Gestational diabetes mellitus in Tanzania - public health perspectives

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Thesis

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Abstract

Background: Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy. Women with GDM are at increased risk for preeclampsia during pregnancy and for delivery complications. In most cases GDM ends after pregnancy, but it increases the risk for future type 2 diabetes, and cardiovascular diseases, to both the mother and the child. With the current increase in prevalence of overweight/obesity and type 2 diabetes in Tanzania and other Sub Saharan African countries, it is possible that GDM may exist and may be on the rise.

Methods: A cross-sectional survey was done in 2011 through 2013 where 910 women in Tanzania (609 from urban, 301 from rural areas) were studied during their usual antenatal clinic visits. Weight, height, mid upper arm circumference (MUAC), blood pressure and haemoglobin levels were measured by a trained technician. Blood glucose was measured at fasting and at two hours after 75 g oral glucose tolerance test. Women were classified as having GDM using WHO 1999 criteria. Sociodemographic information was collected through face-to-face interviews using structured questionnaire or retrieved from the antenatal clinic card. Dietary intake data was collected using 24-hour recall interview and foods were categorised into groups based on dietary diversity. The international physical activity questionnaire (IPAQ) was used to assess activities in the past one week. Information on birth outcome was obtained from 466 urban mothers (response rate 77%) through telephone interviews. To estimate the burden of GDM in the region, we additionally conducted a systematic search of published literature on the prevalence and risk factors of GDM in Sub Saharan Africa. Out of the 22 reviewed studies, 15 studies graded as having low or moderate risk of bias were included in a meta-regression analysis. Finally, a review of literature regarding the health system and antenatal care was done and supported by a survey to assess antenatal care services in 24 health facilities that provide maternal and childcare services in Dar es Salaam region.

Results: The prevalence of GDM was much higher among women residing in the urban (8.4%) compared to those in the rural areas (1.0%), which was much higher compared to 0% reported in the 1990s. Prevalence of GDM was higher for women who had a previous stillbirth, family history of type 2 diabetes and MUAC ≥28 cm, and lower for women with normal haemoglobin concentrations compared to those with anaemia. Likewise, the prevalence of hypertension disorders of pregnancy

(HDP) was higher in urban (8.9%) compared to rural areas (5.3%). Risk factors for HDP in urban women were advanced maternal age, high MUAC, gestional age and being HIV positive, and in rural women age and gestational age.
We reviewed 22 studies conducted in six out of the 47 Sub saharan African countries. Heterogeneity between the studies was high and it could not be significantly explained by study setting, population, diagnostic criteria, or the year the study was done. Nevertheless, a relatively higher prevalence was observed in studies done after the year 2000, when women at risk were selected and when more current diagnostic criteria were used. The prevalence was up to about 14.0% when women with at least one risk factor were studied. In Dar es Salaam women, despite a high prevalence of anemia and HIV, the prevalence of macrosomia was higher (5.9%) compared to the prevalence of low birth weight (3.6%). Presence of GDM (OR 3.46, 95% CI 1.01-11.85) and birth weight of the previous child (OR 2.42, 95% CI 1.17-4.99) were the main predictors of macrosomia and HDP (OR 3.75, 95% CI 1.11-12.68) was the main predictor of low birth weight. Although glucose testing in urine appeared to be universally done in the urban setting, the sensitivity of this test for detection of GDM is low. Therefore selective blood glucose testing should be implemented and HIV testing and counselling may be used as an entry point.
Conclusions: The prevalence of GDM and HDP was higher in the urban compared to the rural areas in Tanzania, indicating an increasing in women who are at risk for delivery complications, poor pregnancy outcomes, type 2 diabetes and cardiovascular diseases in later life. The risk factors observed can be used to identify risk groups for screening and as target for prevention interventions. To inform policy makers and for better health care planning, further studies on the costs for blood glucose testing during the usual antenatal clinic visits and on the management of women with GDM are warranted.

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Chapter 1

General introduction

Background

The prevalence of type 2 diabetes mellitus is increasing globally, and it is estimated that the highest increase between now and 2035 will be in Africa (109%) [1].The increasing prevalence of type 2 diabetes in the African population is linked to an increase in obesity. Most studies have observed a higher prevalence of obesity in women than in men, and significant increases are noted in rural areas [2-5]. This evidence of the increasing prevalence of type 2 diabetes mellitus and obesity begs the question of whether there are more women with hyperglycaemia in pregnancy – a condition that has been shown to result in diabetes and its complications at a later life stage [1].

Gestational diabetes mellitus is defined as carbohydrate intolerance resulting in hyperglycaemia of variable severity, with onset or first recognition during pregnancy. The former WHO definition included previously unrecognized type 2 diabetes mellitus [6]. According to the new WHO recommendation, hyperglycaemia first detected at any time during pregnancy is classified as either diabetes in pregnancy or gestational diabetes [7].

The underlying pathophysiology of gestational diabetes is decreased maternal insulin sensitivity, or increased insulin resistance, which begins near mid pregnancy and progresses in the third trimester to the levels similar to those seen with type 2 diabetes [8, 9]. Insulin resistance is defined as the inability of a defined concentration of insulin to affect a predictable biological response of nutrient metabolism at the level of the target tissue [10]. Insulin resistance appears to result from a combination of increased maternal adiposity and the insulin-desensitizing effects of hormonal products of the placenta [9]. Most cases of GDM result from beta cell dysfunction that occurs from secretions that arise in women with chronic insulin resistance and therefore seem to be related to type 2 diabetes [8, 9]. Insulin resistance is the key to the development of GDM: the main biological difference between women with and without GDM is a failure of insulin to rise in response to insulin resistance resulting from pregnancy. The strong family association between GDM and type 2 diabetes mellitus supports the notion that GDM is an inherent abnormality of the beta cell uncovered by the insulin-resistant state of pregnancy [11].

Usually GDM goes away after the baby is born [8]. Nevertheless, it makes a woman prone to GDM in her next pregnancy and is associated with long-term health risks

to the mother as well as the child, such as a predisposition to obesity, metabolic syndrome, and diabetes later in life [12-15]. A systematic review of 28 studies reported a cumulative incidence of diabetes ranging from 2.6% to over 70% in studies that examined women 6 weeks postpartum to 28 years postpartum [16].The risk was higher in women who required insulin and in those with a high body mass index (BMI) compared to those who did not require insulin or had a low BMI [16, 17]. *As proper management and treatment of GDM prevents future complications, early diagnosis and identification of women at risk is essential.*

Trends and prevalence of GDM

The prevalence of GDM may range from one to 23% of pregnancies depending on the population studied and diagnosis criteria used [18-21]. Ferrara reported that GDM prevalence has increased by 10 to 100% in several ethnic groups during the past 20 years. A significant increase in GDM prevalence was noted in the US and Australia, where a higher relative increase was observed in young women [22, 23]. In urban China, the adjusted prevalence of GDM was reported to have increased by 2.8 times during the years 1999–2008 from 2.4% to 6.8% [24].

Gestational diabetes is also becoming a public health concern in Sub-Saharan Africa (SSA), although there are limited data available on the general population. A study in rural South Africa reported a prevalence of GDM of 1.5% and impaired glucose tolerance (IGT) of 7.3% [25]. In an Ethiopian rural community, GDM prevalence was 3.7% [26]. In Tanzania, there is a paucity of current data on GDM prevalence in rural and urban areas, but about two decades ago, GDM was not detected [27]. More recently, however, it has been suggested that GDM may exist in rural East Africa because 3.1% of children are large for their gestational age [28]. Unlike in most developed countries where blood glucose level is assessed during routine antenatal clinic (ANC) visits, in Tanzania, and probably other SSA countries, priority is given to screening for anaemia, malaria, and HIV. In some clinics, glucose in urine is sometimes assessed. However, due to its low sensitivity and negative predictive value, it is not recommended for diagnostic purposes [29, 30]. If a patient has signs and symptoms of GDM, diagnosis and management may vary from one clinic to another depending on whether the clinic is in an urban or in a rural area, or in a private or a government hospital.

Risk factors for GDM

Risk factors for GDM were summarized by Hayoush et al in 2004 and Petry in 2010 as shown in Table 1.1. The most recognized risk factors include overweight or obesity, advanced maternal age, family history of type 2 diabetes, and history of GDM [19, 31-34].

Table 1.1: Summary of risk factors for GDM

- Obesity
- Advanced maternal age
- Excess weight gain in pregnancy
- Family history of type 2 diabetes or GDM
- Previous history of GDM
- Previous congenital malformation, stillbirth, macrosomic baby, or caesarean section
- Pregnancy-induced or pre-existing hypertension
- Multiple pregnancy
- Birth weight of the mother (high or low)
- Increased iron store
- Polycystic ovarian syndrome
- Glycosuria
- Smoking during pregnancy
- High parity
- Short stature
- High intake of saturated fat
- α-Thalassemia trait

Adapted from Ben-Hayoush et al (2004) and Petry (2010) [35, 36]

Other risk factors include previous macrosomia [13], previous still birth [37, 38], short stature [39, 40], physical inactivity [41], cigarette smoking [42], and dietary factors [43, 44]. In addition, infertility [45] and history of depression [46] have recently been reported as risk factors. There is growing evidence from systematic reviews that maternal birth weight, low or high, is also a risk factor for GDM [39, 47]. A retrospective cohort study in Canada found that alcohol intake was

protective against GDM, although other confounding factors were not taken into account [48].
GDM can vary according to ethnicity/racial differences, with some ethnic or racial groups being at relatively higher risk than others, irrespective of their BMI [49]. A large cohort study on Northern California from 1995 to 2006 examined racial/ethnic disparities in the prevalence of GDM by BMI. The authors reported that age-adjusted prevalence increased with increasing BMI category, but Asian and Filipino women had a GDM prevalence of 9.9% and 8.5%, respectively, at a relatively lower BMI of 22.0–24.9 kg/m^2, whereas other ethnic groups had a high prevalence at a higher BMI category (>28 kg/m^2) [50]. Furthermore, the risk of developing type 2 diabetes also varies according to ethnicity, and in the United States black women have the highest risk, even after adjusting for confounders [51].

Overweight and obesity as a risk for GDM
In several meta-analyses of primarily non-Asian populations, pre-pregnancy BMI has been shown to be the most important risk factor for GDM [52, 53]. Kim (2010) calculated the percentage of GDM attributable to overweight (15.4%), obesity (9.7%), and extreme obesity (21.1%) where the overall population attributable fraction was 46.2% [54]. In a recent meta-analyses of 20 relevant studies published between 1980 and 2006 [53],the risk of developing GDM was approximately 2, 3, and 6 times higher among overweight, obese, and severely obese women, respectively, as compared with normal-weight pregnant women, irrespective of the study characteristics. However, some studies in SSA did not find any association between BMI and GDM [25, 26, 55], probably due to genetics/ethnicity and/or differences in fat distribution [56, 57].

In Tanzania, the prevalence of obesity is increasing, especially in urban areas. For example, the prevalence of overweight and obesity among women attending ANCs in Dar es Salaam increased from 3.6% in 1995 to 9.1% in 2004 [58]. Another cross-sectional study in the urban area (Temeke district) in Dar es Salaam reported that the age-adjusted prevalence of obesity was 13% for men and 35% for women. Likewise, abdominal obesity was much higher in women (58%) compared to men (11%), and women had greater odds of having metabolic syndrome compared to male participants [59]. In Kinondoni district, also in Dar es Salaam, a community survey showed similar results; the overall prevalence of obesity was 19.2%, with more women being obese (24.7%) than men (9.0%) [60].

Obesity is thought to be a problem of affluence, and a higher prevalence is expected in urban compared to rural area. However, recent data show that rural areas are equally affected. A cross-sectional survey in three different seasons in rural Tanzania reported the prevalence of overweight and obesity in women to be 16% and 6%, respectively, which was higher than the prevalence of underweight (7%) [61]. The link between obesity and GDM shows that, with this trend in obesity and overweight in Tanzania, GDM could also exist, contrary to what was reported 20 years ago.

Dietary intake

Several studies have related dietary intake to the development of glucose intolerance in both the general population and pregnant women. In pregnant women, the diet before and/or during pregnancy may be protective or increase the risk for GDM. Large prospective cohort studies reported that pre-pregnancy diet – in particularly a diet low in fibre and high in glycaemic load [62], a high intake of protein, particular red meat[44, 63], or high intake of animal fat and cholesterol [64] – was associated with increased risk for GDM. On the other hand, higher intake of vegetable protein, specifically nuts, was associated with a significantly lower risk [63]. Interventional studies suggest that an increase in both fibre and low glycaemic carbohydrate sources in the diet decreases the pregnancy-associated progression of insulin resistance [65, 66].

There is also growing evidence of an association between micronutrient status and GDM. For example, two studies reported that low maternal dietary vitamin C and low plasma ascorbic acid concentration increased the risk of gestational diabetes [67, 68]. Several studies associated vitamin D deficiency with increased risk of GDM [69-71]. Cho and co-workers reported only severe vitamin D deficiency to be associated with risk for GDM [71], and Parlea et al. found that lower vitamin D status in early pregnancy increased the risk for GDM independent of race, age, season, and maternal weight [70]. However, in a nested case-control study, vitamin D deficiency was not found to be associated with GDM [72]. A case-control study in Sudan compared zinc and selenium levels among women with and without GDM, where the groups were matched in age parity, gestational age, haemoglobin, and BMI. This study reported no correlation between zinc or selenium and blood glucose levels [73].

Observational studies suggest that high iron intake during pregnancy is associated with the risk of GDM. The adjusted relative risk (RR) for GDM associated with a 0.5mg per day increase in iron intake was 1.22 (95%CI; 1.10-1.36). No significant associations were observed between total dietary, non-theme, or supplemental iron intake and GDM risk[74].

There is a growing interest in considering the association between dietary pattern or food group consumption rather than individual food or single nutrient intake [75]. However, there are few studies on the association of dietary intake or dietary diversity with GDM.

Anaemia in relation to GDM

The prevalence of anaemia in pregnant women is estimated to be 38% worldwide. In Tanzania, a study conducted at Muhimbili National Hospital in 2009 reported that 68% of women attending ANCs were anaemic [76]. Maternal high or low haemoglobin concentration during pregnancy has been reported to increase the chance of unfavourable pregnancy outcomes such as low birth weight, preterm birth, and perinatal death [77-79]. Maternal death due to anaemia in Africa is about 3.7% [80]. In Tanzania, maternal death due to anaemia is approximated to scale up to 15% because of malaria [81]. Anaemia is routinely assessed by measurement of haemoglobin (Hb) values during ANC visits, and women with Hb less than 8.5 mg/dl are usually referred to a clinician for further investigation and treatment. Although a low Hb level does not necessarily mean low iron levels, it is general practice to assess Hb levels for anaemia during pregnancy, and in rare cases, just the palms and the eyes are observed. The main cause of anaemia in most SSA countries is iron deficiency, but infections such as malaria, HIV, and parasites also contribute to anaemia during pregnancy [82].

A large body of evidence supports the hypothesis that excess iron contributes to chronic diseases by fostering excess production of free radicals. Elevated body iron stores are associated with increased risk of type 2 diabetes [83], insulin resistance [84], and GDM [85, 86]. Several case-control studies reported high serum ferritin in women with GDM compared to normal women [87, 88]. A case-control study assessing iron status in 34 women with GDM and 34 with normal glucose levels found that all biomarkers of iron status were higher in women with GDM than in their matched controls [89]. Although some studies have attempted to assess whether iron supplementation is linked to disease risk, particularly diabetes in women, the results have been inconsistent [90-92]. The effect of GDM on birth

outcome in Tanzania, where there is a high prevalence of anaemia and HIV infections during pregnancy, is rarely studied.

GDM and birth outcome

The common consequence of uncontrolled hyperglycaemia during the second and/or third trimesters of pregnancy is a high chance of delivery of a macrosomic baby, posing a risk to the mother and the child [93, 94]. Even when birth weights are similar in women with and without GDM, children born to women with GDM have increased body fat compared with infants of women with normal glucose tolerance [95, 96]. These babies are also at increased risk of future type 2 diabetes and other metabolic syndromes during childhood, adolescence, and adulthood; hence the lifecycle of diseases [97, 98]. Maternal outcomes associated with GDM are pregnancy-induced hypertension, preeclampsia, ante-partum haemorrhage, and caesarean section, and other neonatal complications include preterm birth, birth trauma, and congenital anomalies [99]. There is also at least a seven-fold increased risk of developing type 2 diabetes in women with GDM compared to those with normoglycemia[100]. There is a high chance of decreasing these risks if GDM is diagnosed and treated early enough. Randomized trials of glycaemic control in pregnancies complicated by GDM reveal decreased rates of macrosomia and shoulder dystocia among those treated [101, 102]. Early diagnosis and management would therefore reduce the risk of future complications related to GDM, as illustrated in Figure 1.1.

Pregnancy, therefore, provides an important window of opportunity for early identification of high-risk women; thus, there is a need for better planning for prevention interventions at an early stage and for management of GDM.

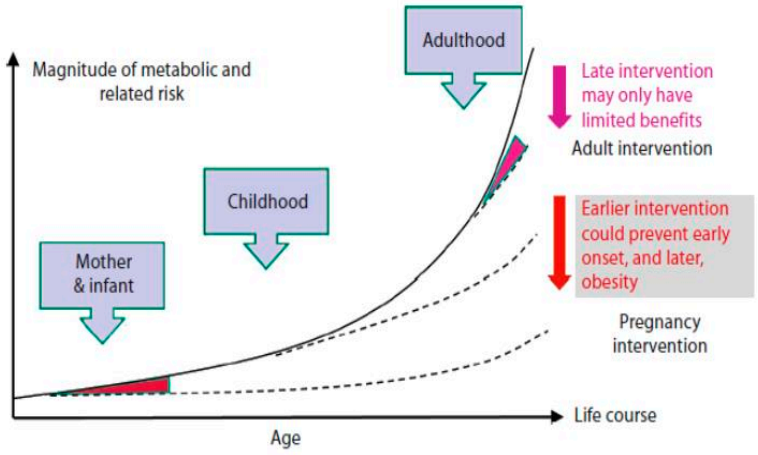

Figure 1.1: Summary of potential lifetime intervention in the mother and/or infant for preventing later adverse outcomes (adapted from Symonds et al 2013) [103]

Hypertensive disorders during pregnancy

Hypertensive disorders during pregnancy (HDP) can be chronic when diagnosed before 20 weeks of pregnancy and persisting for more than two weeks after delivery, pregnancy induced, with or without preeclampsia, or preeclampsia. They usually occur late in pregnancy and are among the main contributors to maternal death in both developed and developing countries [104, 105]. GDM is one of the disorders associated with HDP and it increases the risk for chronic hypertension [106]. Other risk factors such as obesity, advanced maternal age, and multi-foetal pregnancy are common for both GDM and HDP. Like GDM, although non-chronic HDPs can resolve after delivery, they cause significant risk to the mother as well as the foetus and are a determinant of long-term diabetes development especially when they co-exist with GDM. In a population-based Canadian retrospective cohort study where women were followed up for 16.5 years, GDM led to a 12-fold risk increase for type 2 diabetes (hazard ratio (HR) 12.77; 95% CI, 12.44-13.10), but this risk increased further when GDM co-existed with preeclampsia (HR 15.75; 95% CI, 14.52-17.07) or with gestational hypertension (HR 18.49; 95% CI, 17.12-19.96). The risk for diabetes with preeclampsia alone increased 2-fold (HR 2.08; 95% CI, 1.97-2.19), similar to the risk increase with gestational hypertension alone (HR 1.95; 95%

CI, 1.83-2.07) [107]. In Tanzania, it is a requirement to take blood pressure measurements and to assess urine for protein during ANC visits. However, epidemiological studies on HDP and their determinants have rarely been reported.

Screening and diagnosis of GDM

Although the burden of GDM is acknowledged in most parts of the world, to date there are no agreed criteria for GDM screening and diagnosis. Some researchers recommend screening to start as early as 16 weeks of pregnancy [108], with a majority recommending screening at 24 to 28 weeks. Some organizations like the American College of Obstetricians and Gynaecologists (ACOG) and the UK National Institute for Health and Care Excellence (NICE) recommend selective screening based on risk factors [109, 110], whereas others like IADPSG, the Australasian Diabetes In Pregnancy Society (ADIPSI), the American Diabetes Association (ADA), and the Diabetes in Pregnancy Study Group India (DIPSI) recommend universal screening of all women [111-113].

The 'how' aspect is even more challenging, because recommendations for screening and diagnosis vary between medical organizations, and practice varies between health facilities even within the same country [114, 115]. The primary debate revolves around whether screening should consist of only fasting glucose, random glucose, or glucose challenge with 50 grams regardless of the last meal. Diagnostic criteria also vary, from using 100 g glucose or 75g glucose load, to whether to consider one reading or two readings [116]. An overview of the various diagnosis criteria is presented in Table 1.2. The simplest is the Indian guideline, which recommends a single glucose challenge test using 75g glucose load regardless of the last meal. It is reported to be cost effective, patient friendly, and an evidence-based approach to diagnosis of GDM [117]. The new ADA criteria propose either a one-step approach using 75 g of glucose, with plasma glucose measured at fasting and after two hours, or a two-step approach, where 50 g of glucose is given in a non-fasting state followed by 3-hour 100 g glucose for those with blood glucose ≥7.8 mmol/L [118]. In 2013, the WHO reviewed their 1999 recommendation, and the new guideline distinguishes women with previously undiagnosed type 2 diabetes opposed to GDM by setting a different cut-off for fasting and blood glucose levels after a 75 g glucose tolerance test (OGTT) [7]. This means that diabetes in pregnancy is defined as women with previously undiagnosed diabetes or fasting plasma glucose ≥7.0 mmol/L, 2-hour plasma glucose ≥11.1 mmol/L following 75 g OGTT, or random plasma glucose ≥11.1

mmol/L and diabetes symptoms, while lower cut-offs for fasting glucose levels and 2-hour OGTT are used for diagnosis of GDM.

Table 1.2: Different diagnostic criteria used for GDM diagnosis

Organization	Screening test	Blood glucose thresholds	Diagnostic criteria
WHO 1985 [119]	2 hr 75g OGTT	Fasting ≥7.8 mmol/L 2 hr ≥11.1 mmol/L	At least one
WHO 1999 [6]	2 hr 75g OGTT	Fasting ≥7.0 mmol/L 2 hr ≥7.8 mmol/L	At least one
WHO 2013 [7]	2 hr 75g OGTT	Fasting: 5.1-6.9 mmol/L 1 hr ≥10 mmol/L 2 hrs ≥8.5 – 11.0 mmol/L	At least one
IADPSG[112]	75g OGTT	Fasting 5.1-6.9 mmol/L 1 hr ≥ 10 mmol/L 2 hr ≥ 8.5-11.0 mmol/L	At least one
ADA [118]	Two steps Step 1: 50 g (1 hr ≥ 7.8 mmol/L) Step 2 100g OGTT	Fasting 5.3 mmol/L 1 hr ≥ 10.0 mmol/L 2 hrs ≥ 8.6 mmol/L 3 hr ≥ 7.8 mmol/L OR Fasting ≥5.8 mmol/L 1 hr ≥ 10.6 mmol/L 2 hr ≥ 9.2 mmol/L 3 hr ≥ 8.0 mmol/L	Two or more
	One step: 75g OGTT	Fasting ≥5.3 mmol/L 1 hr ≥ 10 mmol/L 2 hrs ≥8.6 mmol/L	At least one
ADIPSI [120]	75g OGTT	Fasting ≥5.1 mmol/L 1 hr ≥ 10 mmol/L 2 hr ≥ 8.5-11.0 mmol/L	At least one
DIPSI [121]	75g OGTT	2 hr ≥7.8 mmol/L	Only one
DPSG/EASD [122]	75g OGTT	Fasting >5.2 mmol/L 2 hr ≥ 9.0 mmol/L	At least one
Carpenter and Coustan[123]	3 hr 100g OGTT	Fasting ≥5.3 mmol/L 1 hr ≥10 mmol/L 2 hr ≥ 8.6 mmol/L 3 hr ≥ 7.8	At least two

NDDG [124]	3 hr 100g OGTT	Fasting ≥5.8 mmol/L 1 hr ≥10.6 mmol/L 2 hrs ≥9.2 mmol/L 3 hrs ≥ 8.0 mmol/L	At least two

WHO: World Health Organization; IADPSG: International Association of Diabetes and Pregnancy Study Group; ADA: American Diabetes Association; DIPSI: Diabetes in Pregnancy Study Group India; ADIPSI: Australian Diabetes Association in Pregnancy Society; DPSG: Diabetes Pregnancy Study Group; EASD: European Association for the Study of Diabetes; NDDG: National Diabetes Data Group

Rationale

About 20 years ago, GDM was not detected in rural and urban Tanzanian communities [27, 125]. Recently, an increase in the prevalence of type 2 diabetes, overweight, and obesity has been reported, with more women being overweight and obese than men [59, 60]. Although this is especially clear for the urban areas, the majority who reside in the rural areas may also be affected because the rural population is also under nutrition transition, i.e. there is increased intake of dietary fats and carbohydrate-rich foods as the main source of energy [61]. Since dietary energy intake, obesity, and diabetes are interlinked, GDM is therefore expected to exist in the Tanzanian community, although rarely studied.

With the current prediction of increasing type 2 diabetes cases, even at a younger age, which could be related to GDM, controlling GDM would be of potential benefit to reduce the health care burden for treating people with type 2 diabetes, which is a costly lifetime condition. Diabetes testing is not a usual practice in Tanzania; priority is given to HIV/AIDS, malaria, and tuberculosis. GDM screening is not conducted in most health centres unless a patient has signs or symptoms of diabetes. Generally, there is limited up-to-date information on the prevalence of GDM, on its risk factors, and on related birth outcomes in Tanzania.

Research questions and thesis outline

Overall objective

The general objective of this study is to determine the prevalence of GDM and its determinants in urban and rural areas in Tanzania and in SSA. To achieve the overall objective, five research questions were formulated:

1. *Is gestational diabetes mellitus present in Tanzania? If yes, what are the determinants?*

As reported in **chapter 2,** 910 pregnant women attending ANCs in Dar es Salaam region representing the urban area (n=609) and in Morogoro region representing the rural area (n=301) area were assessed. Blood glucose levels were checked at fasting state and after a 75gr glucose challenge test.

2. *What is the burden and risk factors for gestational diabetes mellitus in Sub-Saharan Africa?*

As reported in **chapter 3,** a systematic review and meta-regression was conducted by searching published articles from PubMed with a specific search in Google Scholar on the prevalence of, and/or risk factors for, GDM in any of the SSA countries.

3. *What is the prevalence and potential risk factor(s) for hypertension during pregnancy in women attending antenatal clinics in Tanzania?*

The prevalence of hypertension during pregnancy was determined and multiple logistic regression analysis was done to identify potential risk factors for hypertension during pregnancy (**chapter 4**).

4. *What are the maternal risk factors for macrosomia and low birth weight in Tanzania?*

This question is answered in **chapter 5** where, after follow up of 609 urban women after delivery, birth outcome data for 466 women were available.

5. *How is the Tanzania antenatal care system prepared to handle the rising challenge of diabetes in pregnancy?*

This question is answered in **chapter 6**. We reviewed published journal articles and other documents that discussed the quality of ANC in Tanzania and the strategies in place to improve maternal and child health. In addition, we conducted a survey in 12 private and 12 government health facilities located in Dar es Salaam to assess

the current screening practices and views of health care providers with regard to inclusion of blood glucose testing during maternal and childcare services.
Finally, in **chapter 7,** the results of different studies are discussed in a broader context with an emphasis on methodological aspects and public health implications; recommendations and directions for future research are given.

Study site and population

The study was conducted in Dar es Salaam city, representing an urbanized population, and in the Kilombero district in Morogoro region representing a rural area (Figure 1.2).

Location of the study area

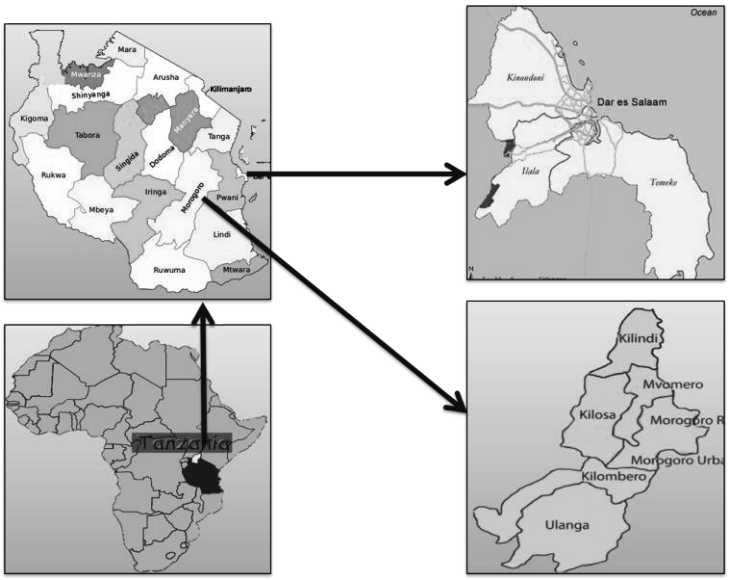

Figure 1.2: Map showing location of the study area, Tanzania

Dar es Salaam is the largest city in the country with a population of about 4.3 million, with the highest annual population growth rate of 6.5%, accounting for 10% of the Tanzania mainland population [126, 127]. The city is situated along the east coast bordering the western side of the Indian Ocean. Administratively, the city has three districts, namely, Ilala, Kinondoni, and Temeke. The districts are divided into

10 divisions, which are subdivided into 93 wards, 448 streets (*mitaa*), and 8 constituencies. The health sector in the region provides health care services through hospitals, health centres, dispensaries, mobile health services, and referrals. The region has 449 health facilities (HFs), of which 28 are hospitals, 29 are health centres, and 392 are dispensaries.

Kilombero is one of the seven districts of Morogoro region, located in South-eastern Tanzania, about 230 km from Morogoro town and 420 km from Dar es Salaam. According to the 2012 population census, it had a total population of 407,880, with an almost equal number of males and females, with a population growth rate of 2.4%,and an average household size of 4.3 [126]. The district has 58 HFs, two of which are hospitals, six are health centres, and fifty are dispensaries.

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Chapter 2

Prevalence of gestational diabetes mellitus in urban and rural Tanzania

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Abstract

Aim: To estimate prevalence of gestational diabetes mellitus (GDM) and associated determinants in urban and rural Tanzania.

Methods: A cross-sectional study was conducted from 2011 through 2012 in selected urban and rural communities. Pregnant women (609 urban, 301 rural), who were not previously known to have diabetes, participated during usual ante-natal clinic visits. Capillary blood samples were collected at fasting and two hours after 75gm glucose load and were measured using HemoCue. Diagnosis of GDM was made using World Health Organization (WHO) criteria.

Results: Women in rural areas were younger (26.6 years) than in urban areas (27.5 years). Mean gestational age, height, and mid-upper arm circumference (MUAC) were similar for the two areas. Overall prevalence of GDM averaged 5.9%, with 8.4% in urban area and 1.0% in rural area. Prevalence of GDM was higher for women who had a previous stillbirth (OR 2.8, 95% CI 1.5-5.4), family history of type 2 diabetes (OR 2.1, 95% CI 1.1-4.2), and MUAC above 28 cm (OR 1.9, 95% CI 1.1-3.3), and lower for women with normal haemoglobin compared with anemia (OR 0.45, 95% CI 0.22-0.93).

Conclusions: Prevalence of GDM is higher than expected in urban areas in Tanzania, indicating an increasing population who are at risk for delivery complications and type 2 diabetes in Sub-Saharan Africa.

Introduction

WHO defines GDM as carbohydrate intolerance resulting in hyperglycemia of variable severity with onset or first recognition during pregnancy [1]. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy. Hyperglycemia usually disappears after the baby is born, but is associated with long term health risks to the mother and the child, such as predisposition to obesity, metabolic syndrome and diabetes later in life [2, 3]. Studies have shown that women with GDM had a 17 to 63% risk to develop postpartum diabetes within 16 years, and the risk is higher in women who required insulin and those with high body mass index (BMI) [4-6].

Prevalence of GDM may range from 1% to 20% of pregnancies depending on the population studied [7-11]. A review by Ferrara showed that GDM prevalence has increased by 10 to 100% in several race groups during the past 20 years [12]. Higher prevalence was observed among US women from Asian and Philippino origin even at a lower BMI [13]. Community based studies have shown that the prevalence of GDM varies across urban, peri-urban and rural areas [9,14]. Factors contributing to GDM include family history of diabetes, age above 25 years and BMI above 25 [15,16]. Other factors include sedentary life style, pregnancy weight gain, maternal height, dietary factors and cigarette smoking [17,18]

Studies on GDM in Sub-Saharan Africa are generally few. In a South African rural community a prevalence of 8.8% was reported and in rural Ethiopia the prevalence was 3.7% [7,19]. In Tanzania, data on the prevalence of GDM in rural and urban areas are scarce. About two decades ago, GDM was not detected in either rural or urban areas [20,21]. Ten years later, however, an increased prevalence of overweight and obesity was reported [22-24]. This implies that the prevalence of GDM may have increased as well, with accompanying increases in delivery complications and risk for type 2 diabetes later in life for the mother and the child.
This cross-sectional study was done to estimate and compare prevalence of GDM in urban and rural communities. It is envisaged that the results of this study will provide essential information regarding the need to treat and prevent GDM in a country where there is also a challenge of combatting communicable infections and other forms of malnutrition as well as changing dietary and lifestyle practices which are risk factors for GDM.

Methods

A cross-sectional study was conducted in Dar es Salaam city and Morogoro region from August 2011 through March, 2012. The study subjects were pregnant women aged 20 years or more and 20 gestational weeks or more, attending antenatal clinic (ANC) at selected six health facilities in Dar es Salaam city (urban) and two centers in Kilombero district in Morogoro region (rural).

Six health facilities in the urban area and two health facilities in the rural area where chosen based on their high number of pregnant women attending ANC. All women aged above 20 years and with gestational age of 20 weeks or more, attending ANC during the survey period, were eligible to participate. Women with previously diagnosed diabetes and women from ethnic groups other than African were excluded. Other exclusion criteria included having chronic disease(s), such as sickle-cell anaemia or cancer, and having conditions that limit activities or normal dietary intake, such as bed-rest since conception. In two health facilities, on some days more women were attending ANC than researchers could handle and on these days, the first 15 women attending that day were included.

During their normal ANC visit, the aim of the study, the procedure and the possible effects of oral glucose tolerance test (OGTT) were explained to the women, emphasizing that participation was voluntary. Tanzanian National Medical Research Institute (NIMRI) approved the study. Informed consent was sought from the study subjects before commencing of the study.

With the assistance from reproductive, child health clinical officer, and the nurse in charge, eligible mothers were selected and invited to participate. In the urban area, 715 mothers were invited, 637 qualified for the examination and 599 completed the OGTT. In the rural area, 400 eligible mothers were invited, 315 qualified for the examination and 301 completed an OGTT. Overall response rates were 89% and 79% in the urban and rural area, respectively.

Laboratory assessment

Blood samples were taken using finger prick with a sterile lancet after cleaning the site with antiseptic alcohol swaps. Blood glucose was measured in capillary whole blood using HemoCue Glucose B-201 (Ängelholm AB, Sweden). On the first visit, mothers were asked to remain fasting overnight and return to the center for fasting blood glucose measurement, after a period of three days with usual eating habits and unrestricted activities. When a women's fasting blood glucose exceeded the WHO limit for diabetes (n=12), they were asked to return a second time for a second fasting glucose measurement. When the fasting level was non-diabetic an

OGTT was carried out. An anhydrous glucose (75 g) in 300 mls of water was given and blood glucose was assessed after two hours. Categorization of the women into GDM and normal was made using WHO diagnosis criteria for GDM (fasting and 2-hour capillary whole blood). All those who met criteria for diabetes mellitus and impaired glucose tolerance (fasting ≥6.1 mmol/L or ≥2-hr 7.8 mmol/L) were classified as having GDM [1]. Women diagnosed with GDM were referred to the physician for further investigation, treatment and counseling.

After taking the capillary blood sample for glucose measurement, another drop was taken for testing haemoglobin (Hb) levels. Hb concentrations were measured using HemoCueHb 201+ Haemoglobin photometer (HemoCue AB, Ängelholm, Sweden) and recorded to the nearest 0.1 g/dl. Women were classified as anemic (<11 g/dl) or normal (≥11 g/dl) using Hb cut-off points suggested by WHO [25]. Further classification was in severe (<7 g/dl), moderate (7 to 9.9 g/dl), mild (10.0 to 10.9 g/dl) and normal (≥11 g/dl).

Women were asked to collect urine on the spot in a provided disposable plastic container. Urine samples were tested within one hour for glucose, ketones, leucocytes and protein using multistix made with color sensitive pads (urine strip 10 C, Dialeb GmbH, Austria).

Anthropometric assessment

Systolic and diastolic blood pressure (BP) was measured from mid-upper-arm of the left side while the respondent was sitting and relaxed for 10 minutes before the actual measurement, using a digital BP device (Microlife BPA100, Widnau, Switzerland). Two readings were taken with an interval of five to ten minutes, and the average systolic and diastolic BP was recorded in mmHg. Mothers with high blood pressure (defined as systolic ≥140 mmHg and diastolic ≥90 mmHg) were referred to see the doctor for further investigations and treatment.

Height was measured without shoes and recorded to the nearest 0.1 cm, using height measuring board (Shorr productions, Maryland USA). Weight was measured to the nearest 0.1 kg using Seca Electronic Scale (Seca, Hamburg, Germany) and mid upper arm circumference (MUAC) was measured using a non-stretchable tape. Only less than half of the mothers could recall their pre-gestational weight. It is suggested that pre-gestational weight can be estimated if weight within fifteen weeks of pregnancy is available [26]. Since most of the women appeared late to the clinic (gestational age at booking ranged 8-32 weeks with the mean of 20 weeks), it was difficult to obtain pre-gestational weight. MUAC is known to be relatively

stable during the course of pregnancy and it was highly correlated with pre-pregnancy BMI [27,28]. Women were, therefore, categorized according to MUAC as normal (MUAC <28 cm) and overweight (MUAC >28 cm). The categorisation based on the assumption that there was a negligible change of MUAC during pregnancy and that BMI = 0.1036*MUAC (mm) – 3.9 as suggested by Khadivzadeh [29].

Socio-demographic data and physical activity

Data on socio-demographic and risk factors were retrieved from the ANC cards (gravida, gestational age based on last menstrual period, HIV status, previous stillbirths), or collected using pre-tested structured questionnaires (marital status, education level, source of income, family history of diabetes, and birth weight of the previous child).

Physical activity was assessed retrospectively by using short form of the International Physical Activity Questionnaire (IPAQ) (revised version 2002) which was translated into Kiswahili. The IPAQ short form is designed and tested for adults (age range 15 to 69 years (IPAQ 2005). The IPAQ short form assess specific types of activity such as walking, moderate intensity activities and vigorous intensity activities. Women were asked to recall their activities from the day of the interview up to seven days backward. Data was reported as metabolic equivalents (METS) according to IPAQ scoring protocol which categorized women into high, moderate and low METS groups.

Data analysis

IBM SPSS Statistics version 19 was used for data analysis. Student's t-test, Mann-Whitney U test and Chi-square test were used for comparing selected characteristics variables between urban and rural women and among those with and without GDM. Variables which were found to be significantly different between the groups with and without GDM were analyzed using multiple logistic regression to determine the adjusted odds ratios. Differences between groups were considered significant if $p< 0.05$.

Results

In total, 910 women were studied (609 in urban and 301 in rural) and 900 participated in an OGTT (599 in urban and 301 in rural) (Table 2.1). Mean gestational age (28.1 weeks), height (155.2 cm), and mid-upper arm circumference (27.2 cm) were similar for the two areas. Women in rural areas were younger (26.7 years) than in the urban areas (27.5 years), were more in the high activity level and

had lower blood pressure levels. Mean fasting blood glucose for women in urban areas (4.6, SD 1.0 mmol/L) was greater than that for women in rural areas (4.0,SD 0.8 mmol/L). Similarly, mean 2-hr blood glucose was greater for women in urban areas (6.1, SD 1.1 mmol/L) than for women in rural areas (5.1, SD 1.1 mmol/L).

Table 2.1: Selected characteristics of women attending ANC in urban and rural areas, Tanzania 2011-2012

Characteristic	Urban (N =609)	Rural (N=301)	P-value
Age (years)	27.5 (5.0)	26.6 (5.3)	0.017
Gestational age (weeks)	28.1 (4.8)	28.2 (5.6)	0.684
Height (cm)	155.3 (6.0)	155.0 (6.2)	0.461
MUAC (cm)	27.3 (3.8)	27.1 (3.3)	0.461
Systolic blood pressure (mmHg)	114.8 (15.2)	111.1 (11.5)	0.001
Diastolic blood pressure (mmHg)	72.5 (11.4)	70.4 (9.5)	0.004
Fasting blood glucose (mmol/L)	4.6 (1.0)	4.0 (0.7)	0.001
2-hour blood glucose (OGTT) (mmol/L)*	6.1 (1.1)	5.1 (1.0)	0.001
Haemoglobin (g/dl)	10.1 (1.6)	10.0 (1.4)	0.119
Education level			
Informal	38 (6.2)	44 (14.2)	0.001
Primary	420 (69.0)	199 (66.1)	
Secondary	131 (21.5)	47 (15.6)	
Post-secondary	20 (3.3)	11 (3.7)	
Source of income			
House works	293 (48.1)	87 (28.9)	0.001
Salary/wage	104 (17.1)	25 (8.3)	
Petty business	209 (34.3)	87 (28.9)	
Agriculture	3 (0.5)	102 (33.9)	
Gravidity			
Prime	171 (28.1)	82 (27.2)	0.241
Second	196 (32.2)	81 (26.9)	
Third	130 (21.3)	69 (22.9)	
Four or more	112 (18.4)	69 (22.9)	
Birth weight of the previous child			
Low birth weight (<2.5 kg)	22 (5.6)	15 (7.7)	0.430
Normal birth weight (2.5 – 4 kg)	316 (80.8)	159 (81.5)	
High birth weight (≥4 kg)	53 (13.6)	21 (10.8)	
Level of physical activity			
High	171 (28.1)	126 (41.9)	0.000
Moderate	314 (61.6)	139 (46.2)	
Low	125 (20.4)	36 (12.0)	

Family history of type 2 diabetes				
	Yes	88 (14.4)	25 (8.3)	0.008
	No	521 (85.6)	276 (91.7)	
Previous still birth				
	Yes	93 (15.3)	34 (11.3)	0.103
	No	516 (84.7)	267 (88.7)	
Alcohol drinking				
	Yes	77 (12.6)	23 (7.6)	0.023
	No	532 (87.4)	278 (92.4)	
HIV status				
	Positive	59 (9.7)	12 (4.0)	0.002
	No	580 (90.3)	289 (96.0)	

Continuous variables are presented as Mean (SD) and categorical variables as absolute numbers (percentage); *N= 599 for urban and 301 for rural groups

Family histories of diabetes, previous still births, alcohol drinking and positive HIV status were more prevalent in the urban than in the rural areas. Agricultural work was the main source of income in the rural women, housework in the urban women. Urban women had a higher educational level. Mean fasting and post-glucose load levels, MUAC and Hb levels did not differ according to gestational age (Table 2.2).

Table 2.2: Mean blood glucose levels, MUAC and Hb according to gestational age

	Gestational age (weeks)			
Variable	≤24 (n=276)	25-29 (n=241)	≥30 (n=393)	P-value
Fasting blood glucose (mmol/L)	4.4 (1.1)	4.4 (0.9)	4.4 (1.0)	0.669
Blood glucose 2-hr OGTT (mmol/L)*	5.8 (1.1)	5.7 (1.2)	5.7 (1.3)	0.816
MUAC (cm)	27.2 (3.6)	27.4 (3.6)	27.1 (3.6)	0.591
Haemoglobin (g/dl)	10.3 (1.5)	10.0 (1.6)	10.0 (1.5)	0.176

Data: mean (SD); * n = 272 for gestational weeks ≤24, 238 for 25 to 29 gestational weeks and 390 for ≥30 gestational weeks

Overall prevalence of GDM (n=54) averaged 5.9% (95% CI: 4.5 - 7.7), with 8.4% (95% CI: 6.3 - 10.9) in urban area and 1.0% (95% CI: 0.2 - 2.9) in rural areas (Table 2.3). When using lower cutoff points for fasting blood glucose levels (5.1 mmol/L)

as suggested by the International Association of Diabetes and Pregnancy Study Groups (IADPSG), overall prevalence of GDM (n=108) is 13.1%, (95% CI: 11.4 – 15.4), with 17.7% (95% CI: 14.9 – 20.9) in urban area and 3.7% (95% CI: 2.0 – 6.5) in rural areas.

Table 2.3: Prevalence of GDM in ANC according to area of residence, Tanzania 2011-2012

		WHO criteria		IADPSG** criteria	
Area	N	Prevalence (%)	95% CI	Prevalence (%)	95% CI
Overall	910	5.9	4.5 - 7.7	13.1	11.4 – 15.4
Rural	301	1.0*	0.2 - 2.9	3.7	2.0 – 6.5
Urban	609	8.4*	6.3 - 10.9	17.7	14.9 – 20.9

Data: n (%)

* Comparing urban and rural GDM prevalence: p<0.001

** Prevalence estimated using fasting blood glucose cutoff according to IADPSG (≥5.1 mmol/L).

Mean and standard deviation of fasting glucose was 6.3 (SD 1.7) mmol/L for the GDM group and 4.3 (SD 0.8) mmol/L for the non-diabetic group (Table 2.4). Additionally, mean 2-hr glucose level was 8.2 (SD 1.6) mmol/L for the GDM group and 5.6 (SD 1.0) mmol/L the non-diabetic group. Glycosuria was observed in only two mothers, who were also identified as GDM using fasting blood glucose levels. Out of the 54 GDM cases eight, were identified based on fasting blood glucose levels only (twice fasting blood glucose ≥ 6.1 mmol/L). The others were identified with fasting blood glucose ≥ 6.1mmol/L and/or 2 hour blood glucose ≥ 7.8 mmol/L.

Table 2.4: Mean blood glucose levels at fasting and after oral glucose tolerance test among women without and with GDM

Category	Normal (N = 856)	GDM (N = 54)	P-value
Fasting BG (mmol/L)	4.3 (0.8)	6.3 (1.7)	0.000
BG 2-hr OGTT (mmol/L)	5.6 (1.0)	8.2 (1.6)	0.000
Identification procedure of the 54 women with GDM			
		n	%
Two FBG ≥ 6.1mmol/L, No OGTT		8	14.8
One FBG ≥ 6.1mmol/L, RBG >11mmol/L		2	3.7
FBG ≥ 6.1mmol/L and BG 2 hr OGTTG < 7.8 mmol/L		12	22.2
FBG <6.1mmol/L and BG 2 hr OGTT ≥7.8 mmol/L		25	46.3
First fasting ≥ 6.1mmol/L, Second fasting <6.1mmol/L, BG 2 hr OG TT≥7.8mmol/L		7	13.0
Total		54	100

Mean blood glucose levels (SD)
FBG: fasting blood glucose
RBG: random blood glucose levels
BG 2 hr OGTT: blood glucose two hours after OGTT

Prevalence of GDM was not significantly associated with mothers' age, level of physical activity, gestational age, and gravida, birth weight of the previous child or previous caesarean section (Table 2.5). GDM showed an inverse association with Hb levels, with a higher prevalence in women with anemia (6.7%) compared to those without anemia (3.9%). GDM was more prevalent in women with MUAC ≥28 cm (8.0% vs 4.6%, p = 0.030), a positive family history of type 2 diabetes, (11.2% vs 5.3%, p = 0.007) and in those with a previous still birth (12.6% vs 4.9%, p <0.001).
To establish the independent association of these variables with GDM, we used multiple logistic regression. This showed that previous stillbirth was independently associated with a 2.8 times elevated risk of GDM (OR 2.8, 95% CI: 1.5-5.4). For a positive family history of type 2 diabetes the adjusted OR was 2.1 (95% CI: 1.1-4.2), and for high MUAC (≥ 28cm) 1.9 (95% CI: 1.1-3.3). Women with normal haemoglobin levels had a reduced risk of GDM compared to women with anaemia (adjusted OR 0.45, 95% 0.22-0.93).

Table 2.5: Number of prevalence cases of GDM in selected risk categories, Tanzania 2011-2012

Variable		Normal (N = 856)	GDM (N =54)	P value
Age (years)				
	< 25 years	302 (94.7)	17 (5.3)	0.755
	25 - 29 years	292 (94.2)	18 (5.8)	
	≥30 years	262 (93.2)	19 (6.8)	
Gestational age (weeks)				
	≤24 weeks	257 (93.1)	19 (6.9)	0.722
	25 - 29 weeks	228 (94.6)	13 (5.4)	
	≥30 weeks	371 (94.4)	22 (5.6)	
Gravidity				
	Prime	236 (93.3)	17 (6.7)	0.834
	two	262 (94.6)	15 (5.4)	
	three	189 (95.0)	10 (5.0)	
	≥four	169 (93.4)	12 (6.6)	
MUAC (cm)				
	(MUAC <28cm)	524 (95.4)	25 (4.6)	0.030
	(MUAC ≥28cm)	332 (92.0)	29 (8.0)	
Level of physical activities				
	High	285 (96.0)	12 (4.0)	0.243
	Moderate	422 (93.2)	31 (6.8)	
	Low	149 (93.1)	11 (6.9)	
Birth weight of the previous child (kg)				
	Low birth wt. (<2.5kg)	36 (97.3)	1 (2.7)	0.648
	Normal (2.5 - 3.9kg)	448 (94.3)	27 (5.7)	
	Large birth wt (≥4kg)	71 (95.9)	3 (4.1)	
Previous Caesarean section				
	Yes	55 (91.7)	5 (8.3)	0.250
	No	528 (95.1)	27 (4.9)	
Previous still				
	Yes	111 (87.4)	16 (12.6)	0.001
	No	745 (95.1)	38 (4.9)	

Family history of diabetes				
	Yes	100 (88.5)	13 (11.5)	0.007
	No	756 (94.9)	41 (5.1)	
Anaemia				
	Anaemia (Hb<11g/dl)	601 (93.3)	44 (6.7)	0.098
	Normal (Hb ≥ 11 g/dl)	248 (96.1)	10 (3.9)	

Data: Given as absolute numbers (percentage)

Discussion

The main objective of this study was to assess prevalence of GDM and associated risk factors in urban and rural Tanzania. Prevalence of GDM was higher in the urban community, and much higher than observed in 1993.

We used WHO criteria including fasting and 2-hr glucose levels, because this was more cost- effective and more applicable to our field setting than other criteria. According to WHO, GDM is considered present if capillary fasting blood glucose is ≥ 6.1 mmol/l (110 mg/dl) or 2-hour glucose load ≥7.8 mmol/l (140 mg/dl) [1]. The American Diabetes Association (ADA) recommends two or more positive results: fasting blood glucose above 5.3 mmol/l (95 mg/dl)), 1 hour 75-g oral glucose load of 10 mmol/l (180 mg/dl) or 2 hour of >8.6 mmol/l (155 mg/dl) [30]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed the cutoff point for fasting normoglycemia to be < 5.1 mmol/l (92 mg/dl) and 2 hour after 75 gm glucose load to be less than 8.5 mmol/l (155 mg/dl) [31, 32]. A recent review concluded, however, that both WHO and IADPSG criteria similarly identified women at risk for adverse pregnancy outcomes, but that higher inconsistencies between studies were seen for IADPSG criteria [33]. This may be due to the low fasting glucose cutoff proposed by IADPSG. It is important to note that using IADPSG criteria, our prevalence would be more than two times higher than observed currently using WHO criteria.

GDM is increasing in most countries around the world, the prevalence more likely to occur in older women, those with family history and high BMI, and varying among racial or ethnic groups [11,12]. In our study, overall prevalence of GDM was 5.9%. This shows a large increase since the 1990's, where 0% was reported in studies done in rural and urban Tanzania [20,21].

Our result for the rural area indicates a low prevalence, 1%, compared to other studies in Sub-Saharan Africa. Higher prevalence were found in rural communities in South Africa (8.8%), Ethiopia (3.7%); and also in India (6.7 and 9.9%) [7,9,14,19]. The Ethiopian study, however, was done in a rural minority which suffered from

famine and droughts for long time, hence mothers had persistent chronic malnutrition which may have resulted in intrauterine growth retardation and subsequent high GDM risk [19]. A higher prevalence (11.6%) was reported for urban setting in Nigeria, where women attending ANC during their third trimester were screened using WHO criteria [34].

In general, the prevalence in our urban population is similar to that reported for developed countries [12]. Differences between rural and urban areas have been reported before, for example in India, where the overall prevalence of GDM was 13.9%, varying between the urban (17.8%), peri-urban (13.8%) and rural areas (9.9%) [9].

In our study the biggest difference between the rural and urban women was in educational level and occupation. About one third of the rural women were engaged in agriculture, which is energy intensive activity compared to urban mothers who were mostly doing light house works. Also a study in Cameroon reported higher physical activity energy expenditure by rural compared to urban population [35]. It is likely that changes in dietary habits and sedentary life styles observed in developing countries are responsible for the increase in obesity and metabolic syndrome [22, 36], as well as for the increase in GDM as we observed in Tanzania. Notably, the association of GDM and physical activity was not significant, possibly due to the method used to collect physical activity data. IPAQ was validated in African adult population [37], but not in pregnant women. Additionally, most of our women reported to have changed their activity pattern since they became pregnant. Higher physical activity level before or in early pregnancy was shown to be associated with reduced risk of GDM [38], but was not asked for in detail in our study.

High GDM prevalence was observed in mothers with family history of type 2 diabetes, previous stillbirth, high MUAC and anemia. Several other studies reported positive family history of type 2 diabetes to be associated with GDM [10,11]. In developing countries, however, most diabetic patients especially in the rural areas, die undiagnosed [22], hence more people could have unknown genetic disposition to diabetes, and we probably have underestimated the genetic potential. High MUAC is a reflection of high BMI [27]. We used it because BMI could not be estimated for most of the women, as they did not know their pre-pregnancy weight.

In addition, we observed that the prevalence of GDM was relatively higher in women with Hb< 11 g/dl. This was in contrast with other studies reporting that prevalence of GDM was reduced in women with low haemoglobin levels [39, 40]. However, in our population anemia was highly prevalent; 70% of the women had Hb levels lower than 11 g/dl. The most common cause of anemia in pregnant women in developing countries is iron deficiency [41]. Generally, diabetes is more often associated with iron overload, or hemochromatosis [42]. However, we cannot exclude that iron deficiency anemia is accompanied by other micronutrient deficiencies, like zinc deficiency, which may contribute to development of diabetes [43]. It is also possible that high observed anemia rate is caused by malaria [41], and our results reflect the co-occurrence of GDM and infections. Although advanced maternal age, gestational age, gravidity and macrosomia are known determinants of GDM [44], no clear association between GDM and these risk factors was observed.

Our study was cross-sectional in nature and screening was done during ante natal clinic visits. Women were not followed until delivery, and women who might have un-diagnosed type 2 diabetes were classified as having GDM; however, these were likely few. We excluded women who were teenagers and who were less than 20 weeks pregnant at time of the survey. GDM was, however, detected even in women aged less than 25 years and those with gestational age below 24 weeks, which indicates that universal screening, could be appropriate in the Tanzanian urban population.

Conclusion

The prevalence of GDM is higher than expected in the urban community in Tanzania. Although it is difficult to compare prevalence with other countries due to variations in screening methods and diagnostic criteria, there is a general observation that prevalence of GDM is increasing in Sub Saharan Africa. Proper planned screening, care and prevention strategies for GDM would improve maternal and child care and prevent future increase in type 2 diabetes in the country.

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Chapter 3

Gestational Diabetes Mellitus in Sub Saharan Africa: A Systematic Review and Meta-Regression on Prevalence and Risk Factors

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Abstract

Aim: The prevalence of gestational diabetes mellitus (GDM) is increasing in most parts of the world, but less is known on the trend in Sub Saharan Africa (SSA). We therefore systematically reviewed publications on prevalence and risk factors for GDM in this region.

Methods: We conducted a systematic search in PubMed and reviewed articles published until June 2014 and searched the references of retrieved articles. We explored sources of heterogeneity among prevalence proportions with meta-regression analysis.

Results: In 1069 articles retrieved, 22 studies conducted in six out of the 47 SSA countries were reviewed; half of them were from West Africa, specifically Nigeria. High heterogeneity between the studies was noted, which could not be significantly explained by study setting, population, diagnostic criteria, or time trend but we observed a relatively higher prevalence in studies done after the year 2000, when women at risk were selected and when more current diagnostic criteria were used. Risk factors reported in more than one studies were overweight and/or obesity, family history for Type 2 diabetes, GDM in previous pregnancy, previous still birth, previous macrosomic child and age >30 years.

Conclusions: There are few studies on prevalence and risk factors for GDM in SSA and heterogeneity is high. Prevalence was up to about 14% when high-risk women were studied. Preventive actions should be taken to reduce the short and long-term complications related to GDM in SSA.

Introduction

Recently, the global prevalence of hyperglycaemia in pregnancy in women 20-49 years was estimated to be 16.9% and affecting 21.4 million live births, in 2013, and more than 90% of cases are estimated to occur in low and middle income countries [1]. The prevalence varies depending on the population and diagnostic criteria used. For example, it can be up to 100% higher when International Association of Diabetes in Pregnancy Study Group (IADPSG) criteria is used compared to 1999 WHO criteria [2, 3]. Regarding the estimated number of cases of hyperglycaemia in pregnancy, Africa ranks second after South East Asia [1]. Gestational diabetes mellitus (GDM) is the common cause of hyperglycaemia in pregnancy, accounting for about 90% of all diabetes during pregnancy [4]. Usually GDM goes away after the baby is born [5], nevertheless, it makes a woman prone to GDM in later pregnancies, and is associated with long term health risks to the mother as well as the child, such as predisposition to obesity, metabolic syndrome and diabetes later in life [6-9]. It is also associated with maternal and perinatal outcomes including pregnancy induced hypertension, preeclampsia, ante-partum hemorrhage, caesarean, preterm birth, birth trauma and congenital anomalies [10]. Like with type 2 diabetes mellitus, the highest prevalence in GDM may be seen in urban areas, partly due to increased overweight and obesity, and changes in dietary and physical activity patterns.

Understanding the prevalence and the risk for GDM in Africa may provide evidence on how interventions should be targeted to reduce the magnitude of the problem, to improve maternal and child health and to reduce the burden of Type 2 DM in the region.

A 2011 review on diabetes in Sub Saharan Africa (SSA) included the prevalence of gestational diabetes and reported it to range from 0% to 9% based on five studies, the latest one being published in 2007 [11]. A more recent review on the prevalence of GDM in Africa reported data from 14 studies conducted in six African countries, and reported the prevalence to range from 0% in Tanzania to 13.9% in high risk women in Nigeria [12]. However, these reviews did not investigate the sources of heterogeneity between the studies. In addition, risk factors were not addressed.

We conducted a systematic review of literature to assess prevalence and trends of GDM, and to examine associated risk factors in published articles from original research conducted in SSA.

Methods

Search strategy and study selection

We conducted a systematic literature search for published papers on gestational diabetes in SSA in PUBMED database, published until June 2014. A comprehensive key word search strategy for related terms associated with diabetes and pregnancy and Sub Saharan Africa, Sub-African region or country specific were used without language restriction (Appendix 3.1). To expand the search, wildcard symbol "*****" was used and the search words or phrases were combined using Boolean operators. We included original published articles, short communications and letter to the editor for studies conducted in SSA and in humans, reporting prevalence and or risk factors for GDM in any SSA countries regardless of screening and diagnostic criteria used, and regardless of method used for selection of participants. Studies, which reported only type 1 and or type 2 diabetes, were excluded. A manual search for additional studies was done using references cited in the reviewed articles.

Retrieved articles were transferred to EndNote library X7 where sorting for duplicates was performed. Titles and abstracts were screened by one author (AM) and when decision could not be made through the abstract alone, full articles were acquired for the third stage of screening. Full articles were examined for inclusion by two authors (AM, EF); disagreement was settled by discussion through joint review of the article. Two articles in French, reporting results of the same study, were translated by one investigator and reviewed for inclusion by the two authors. However, they were excluded as information to establish prevalence and diagnostic criteria was lacking. Number of articles not meeting inclusion criteria and reasons for exclusion are shown in Figure 3.1 and details in Appendix 3.2. When more than one article reporting similar results were retrieved, the most informative article was included. Authors were contacted to provide extra information, such as on sampling procedure, the year the study was done and or study setting, when deemed necessary.

Data extraction

The main findings regarding prevalence and risk factors for GDM were summarized by two authors in a prepared excel sheet under subheadings agreed upon by all

authors. The subheadings included study title, name and contact details for first author, country, year when the study was conducted (i.e. year study ended), year of publication sample size, study design, setting, study population, selection of participants, mean age, mean gestational age, exclusion criteria, screening method (random, fasting or OGTT), diagnostic criteria used, prevalence (including 95% CI), risk factors and key conclusion(s). When a single study reported more than one prevalence proportion, based on e.g. study setting or subsample, or compared diagnostic criteria, data were extracted separately and each was considered as separate study in meta-regression analysis. We used the definition of GDM according to WHO: carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy [13]. Prevalence proportions and confidence intervals (CI) reported by each study were recorded or calculated from the given information whenever necessary using spreadsheets for analysis of Epidemiologic Data by Rothman 2005 (version of Nov 10, 2005). We followed the PRISMA checklist (Appendix 3.3) for reporting of systematic reviews [14]. We developed a review protocol and immediately started the review; the protocol was not registered.

Risk of bias

Two reviewers assessed the studies included for the risk of bias independently and any disagreement was resolved through a discussion until they reached consensus. We adopted a risk of bias tool developed by Hoy et al [15] and modified it to suit to our study. The tool consists of ten items that assess sampling, attrition, measurement and reporting bias (Appendix 3.4a). The validity of methodology, appropriateness and reporting of results were assessed, and whenever the information provided was not enough to assist in making judgement for a certain item we agreed to grade that item with a "NO" meaning high risk of bias. Each article was graded as either with low, moderate or high risk of bias depending on the number of items judged "yes". We included all articles in the synthesis of results but only articles judged to have low or moderate risk of bias were included in meta-regression analysis (Appendix 3.4b).

Statistical analysis

We first performed arcsine transformation of the prevalence proportions to handle the distribution asymmetry [16]. Arcsine transformation was preferred to logit transformation because with very small prevalence proportions that approaches

zero, variance for proportions tend to be magnified, hence variance instability would persist even after logit transformation [16]. We used the random effect model to estimate prevalence proportion and the 95% CI. Heterogeneity between studies was assessed using I^2 statistics [17]. In order to identify possible sources of heterogeneity among prevalences, mixed effect meta-regression models were used [18]. The variables considered were year the study/survey was completed (as a continuous variable); study setting (rural and mixed or urban), gestational age of the studied population during diagnosis (all trimesters or ≥24 weeks), diagnostic criteria (older and relatively recent), and population included (general or high risk). The older criteria included O'Sullivan, NDDG, WHO 1985 and own, while the more recent ones were ADA 2002, 2010, WHO 1999 and EASD. All statistical analyses were performed using R Studio 0.98 program utilizing R statistical language version 2.15.3 using Metafor commands.

Results

A total of 1064 single articles and five articles from manual search were retrieved and transferred to EndNote library. Titles and abstracts were screened and 1031 articles were excluded because they were either irrelevant, conducted outside SSA, referred to other types of diabetes or reviews (Figure 3.1). Thirty-seven articles were accessed as full paper and finally 22 articles of studies conducted from 1969 to 2014 were included in the review (Table 3.1). Six articles reported more than one prevalence proportion (three compared less risk with high-risk groups, two compared diagnostic criteria and one compared rural and urban populations).

With respect to risk of bias, ten studies were considered to have low risk of bias (45.5%), five (22.7%) were classified as having moderate risk of bias and seven studies (31.8%) had high risk of bias (Table 3.1 & Appendix 3.4b).

Of all the included studies, eleven were conducted in West Africa, five in South Africa and six in East and Central Africa. Characteristics of included studies are shown in Table 3.1. Sample size for the individual studies ranged from 58 in a prospective cohort in urban Tanzania [19] to 12,030 in a retrospective review of delivery registries in Nigeria [20].

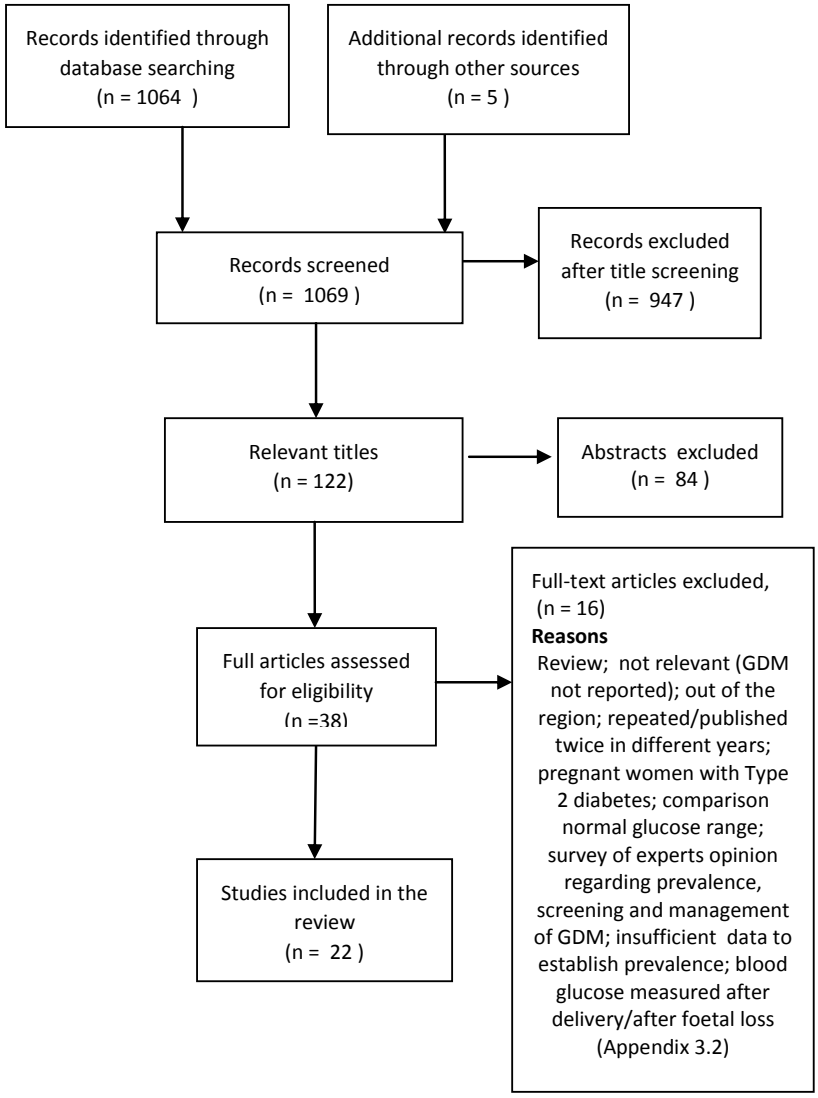

Fig 3.1: Flow diagram for selection of the studies and reasons for exclusion

Table 3.1: Prevalence/Incidence of GDM in SSA by country, setting, mean age, mean gestational age at diagnosis, screening and diagnosis criteria

Studies done in West Africa

Author/year of publication (year study was conducted)	Country	Sample size (response rate)	Setting	Sampling frame	Study design	Mean age/range (years)	Mean gestational age/range (wks)	Screening criteria	Diagnosis criteria	Prevalence (95% CI)	Remarks (risk of bias)
Abudu & Kuti (1987) (1981/1982)	Nigeria	336 (87%)	Urban (Lagos) University hospital	Tertiary hospital	Cross sectional	27	All trimesters	Random BG and 50g GCT (1 hr BG >7.2 Mmol/L)	Fasting BG and 50g OGTT* (O'Sullivan)	1.5% (0.5 – 3.3)	Low
Wokoma *et al.* (2001) (1998/2000)	Nigeria	5026 (NR)	Urban (Port Harcourt) University hospital	Tertiary hospital	Descriptive cohort	31	24 (8-36)	Fasting BG and Urine dipstick test	Own criteria and O'Sullivan**	0.3% (0.2–0.5)	Moderate
Ozumba *et al.* (2004) (1990/1999)	Nigeria	12030 (NR)	Urban (University of Nigeria) University hospital	Tertiary hospital	Retrospective review of delivery registry (10 yrs)	15 to 54	≥ 28	risk factors***	WHO 1999	Overall: 1.7% (1.4-1.9) GDM: 1.0% (0.8-1.2)	High
Olarinoye *etal.* (2004) (1997/1999)	Nigeria	248: 138 WHO criteria and110 NDDG criteria (84.6%)	Urban (Lagos) University hospital	Tertiary hospital	Prospective cohort	31 (18 to 41)	≥ 28 (third trimester only)	NR	WHO 1985 NDDG 1979	WHO: 11.6% (7.0-17.8) NDDG: 4.6% (1.7-9.8) Overall: 8.5% (5.4 – 12.8)	Low

Adegbola & Ajayi (2008)[a] NS	Nigeria	222: 113 in at risk group (84.3%) 109 in normal group (81.3%)	Urban (Lagos) University hospital	Tertiary hospital	Prospective cohort	32 (19 to 45)	24-32	50g GCT (1 hr BG ≥7.2Mol/L)	ADA (2002)	At risk group: 6.2% (2.7-11.9) Normal group: 4.6% (1.7-9.9)	Low
Kamanu *et al.* (2009)[b] (1999/2003)	Nigeria	9040 available for analysis (96.4%)	Urban (state University) University hospital	Tertiary hospital	Retrospective review of hospital records	Normal: 27.1 (19-45) macrosomic: 30.5 (19-45)	24-28	50 gm GCT (1 hr BG ≥7.8 Mmol/L	1 hr after 50 g >7.8mmol/L or 1 hr 75 g OGTT >10mmol/L or 2 hrs 75g OGTT >8.6mmol/L	Overall: 1.5% (1.3-1.8)	High
Kuti *et al*. (2011)[c] (2007/2009)	Nigeria	765 (NR)	Urban (Ibadan) University hospital	Tertiary hospital	Retrospective review of hospital records	32	4-40	risk factors	WHO 1999.	13.9% (11.5-6.4)	Moderate
Ugboma *etal*. (2012)[d] (2006/2009)	Nigeria	960 (49.8%)	Mixed (urban, semi-urban and rural)	Tertiary, secondary and primary hospital and maternity homes	Case control	30	24-34	Risk factors and 50g GCT (1 hr BG ≥7.8mmol/L)	WHO 1999	5% (3.8-6.4)	High

Ewenighi *et al*. 2013) (2010/2011)	Nigeria	250 (NS)	Rural (Three centres in Ebony State)	Three antenatal clinics	Cross sectional	30 (15 to 44)	All trimesters (mean 26)	NR	NDDG (1979)	4.8% (2.6-8.0)	Low
Anzaku & Musa (2013) (2009)	Nigeria	253 (95.5%)	Urban (Jos) University hospital	Tertiary hospital	Cross sectional	31 (19-42)	26 (24-28)	50g GCT (1 hr BG ≥7.8 mmol/L	WHO 1985	8.3% (5.2-12.4)	Low
Fawole *et al*. (2014)[e] (2007)	Nigeria	1086: with risk: 530 (98.7%) General population : 530 (96.9%)	Urban (Ibadan) University hospital	Tertiary hospital	Cross sectional (prospective and retrospective)	30.3	22 (24-28)	Risk factors	WHO 1999	With risk: 4.9% (3.2-6.9) General population 1.6% (0.8-2.9)	Moderate
Studies done in South Africa											
Author/year of publication	**Country**	**Sample size**	**Setting**	**Sampling frame**	**Study design**	**Mean age/range**	**Mean gestational age/range**	**Screening criteria**	**Diagnosis criteria**	**Prevalence (95% CI)**	**Remark (risk of bias)**
Notelovitz (1969)[f] (NS)	South Africa (Indian women)	566 without risk: 301 with risk: 265 (NR)	Durban (Indians) King Edwards Hospital	Tertiary hospital	Cross sectional	NS	All trimesters	NS	(Venous blood taken at fasting and two hrs after 100g OGTT).	Without risk: 8.3% (3.6-11.8) With risk 23.8% (18.9-29.2)	High

Jackson & Coetzee (1979)[g] (1977/1978)	South Africa	558 (NR)	Urban (Cape town) Mixed ethnicity	ANC at Groote Schuur Hospital Secondary/tertiary hospital	Prospective cohort	NS	All trimesters	Risk factors	50 g GCT***	Diabetic 3.0% (1.8-4.7)	Moderate
Ranchod *et al.* (1991) (1987/1988)	South Africa (Indian and collared minority)	1717 (NR)	Urban (Indians and coloured minority)	Northdale Hospital, Pietermaritzburg Secondary/tertiary hospital	Prospective descriptive	NS	All trimesters	75g (1 hr BG ≥7.8mmol/L)	WHO 1985 DPSG/EASD **** DPSG: 1.6% (1.0-2.2)	WHO: 3.8% (2.9-4.8)	Low
Mamabolo *et al.* (2007) (1999/2000)	South Africa	262 (95%)	Rural (Limpopo) Bantu	9 Randomly selected local ANC	Cross sectional	26 yrs	>28 (28-36)	NR	WHO 1999	8.8% (5.6-12.9)	Moderate
Basu *et al.* (2010)[h] (2006)	South Africa	767 (NR)	Urban Johannesburg (mixed ethnic group)	CMJA Hospital, Johannesburg Secondary/tertiary hospital	Retrospective review	Median age 27 yrs (13 to 31)	Median 28 (23 – 32)	Institutional Protocol (fasting BG >8.0 mmol/L or random > 11 mmol/L	Institutional Protocol (Pre-and post-meal BG levels for 6 times within 24 hrs)	1.8% (1.0-2.9)	High

Studies done in East and Central Africa

Author/year of publication	Country	Sample size	Setting	Sampling frame	Study design	Mean age/range (years)	Mean gestational age/range (wks)	Screening criteria	Diagnosis criteria	Prevalence (95% CI)	Remarks (risk of bias)
Swai *et al.* (1991) (1989)	Tanzania	189 85%	Rural community survey	Community survey (8 villages)	Cross sectional	27.5 (>14)	All trimesters (4 to 42)	NR	WHO 1985	0.0%	Low

Lutale *et al.* (1993) (1990)	Tanzania	58 (65%)	Urban ANC	NS	Prospective cohort	23 (15 to 44)	≤14, 14-29 and ≥30	NR	WHO 1985	0.0%	High
Seyoum *etal.* (1999) (1996)	Ethiopia	890 (95%)	Rural (communit y survey)	Community (18 randomly selected villages)	Cross sectional	27 yrs (15-50)	≥24	NR	WHO 1985	3.7% (2.5-4.9)	Low
Jao *et al.* (2013) (2013)	Cameroon	316 (NR)	Semi urban clinic	Community ANC	Cross sectional	15-50 (30.5)	≥24 (24 – 28 wks or first visit for those who booked late)	NR	ADA 2010	6.3% (4.0-9.4)	Low
Tandu-Umba & Muela (2013) (2011)	Congo	108 (NR)	Urban (University hospital)	Tertiary hospital	Cohort	30	28 (24-32)	NR	WHO fasting BG only	7.4 (3.5-13.6)	High
Mwanri *et al.* 2014) (2011/2012)	Tanzania	609 (94.0%)	Urban (ANC)	Six ANC	Cross sectional	28 (20-40)	28 (20-38)	Fasting BG	WHO 1999	WHO 1999: 8.4% (6.3-10.9)	Low
		301 (95.5%)	Rural (ANC)	Two ANC	Cross sectional	27 (20-43)	28 (20-38)	Fasting BG	WHO 1999	WHO 1999: 1.0% (0.2-2.9)	Low

*50g after 12 hrs fasting

**Persistence glycosuria at least two occasions; fasting BG 5.8mmol/L on at least two occasions; 2 hrs BG after 50g OGTT >7.8mmol/L; Diabetic pattern as recommended by O'Sullivan; History of GDM in previous pregnancies (Any three of the listed criteria)

***Fasting >5.5 mmol/L; 1 hr BG after 50g OGTT > 10.0mmol/L; 2 hrs BG after 50g OGTT >6.7mmol/L (any two values)

****Fasting BG >5.2 mmol/L and or 2 hrs BG after 75g OGTT > 9mmol/L.

[a]Family history of Type 2 diabetes in first degree relative, previous macrosomia, previous GDM; BMI ≥30kg/m^2, history of stillbirth, unexplained perinatal death, spontaneous abortion, new-born pathophysiology conditions, previous history of congenital malformations, glycosuria in two or more occasions.

[b]Previous GDM, family history of Type 2 diabetes in first degree relative, obesity, previous macrosomia, previous unexplained intrauterine death, previous baby with gross congenital malformation, polyhydramnios, large baby in the index pregnancy

[c]History of fetal macrosomia or fetal anomalies, obesity, first degree relative with diabetes mellitus, previous intrauterine fetal death, glycosuria and history of GDM in a previous pregnancy

[d]Obesity, failure to gain weight in pregnancy/maintain pre-pregnancy weight, polyhydramnios confirmed by ultrasonic scan, family history of diabetes in first degree relative, previous adverse obstetrical history, history of glucose intolerance, previous macrosomia, repeated miscarriage without a clear cause, unexplained repeated stillbirth

[e] Family history of Type 2 diabetes in first degree relative, previous unexplained stillbirth, recurrent pregnant losses, history of previous congenital abnormality, maternal weight ≥90kg, heavy glycosuria, previous macrosomia, history of GDM, macrosomia in index pregnant, unexplained polyhydramnios

[f]Family history diabetes, unexplained stillbirth or neonatal deaths, glycosuria, history of macrosomic baby, history of progressive increase in birth weight of infants

[g] Diabetes in parent or sibling, repeated miscarriages, weight >=80kg, previous infant weighing >=4000g, previous perinatal death, fasting or repeated postprandial glycosuria, polyhydramnios, previous hyperglycaemia, previous infant with congenital anomaly, Indian ethnic origin

[h]Previous macrosomia, previous stillbirth, previous GDM, persistent glycosuria

NR: Not reported; BG: Blood glucose; WHO: World Health Organisation; NDDG: National Diabetes Data Group; DPSG: Diabetes in Pregnancy Study Group

ADA: American Diabetes Association; EASD: European Association for the Study of Diabetes

IADPSG: International Association of Diabetes and pregnancy Study Groups

Study characteristics and prevalence of GDM according to region.

West Africa: All the 11 studies published from1987 to 2014 were conducted in Nigeria. Most of these studies (9 out of 11) were done in tertiary university teaching hospitals [20-28]. The remaining two studies were done in selected clinics [29, 30]. One study compared prevalence using WHO and NDDG diagnostic criteria [23]; two studies compared women with and without risk factors [27, 31], and one study compared prevalence among women with and without macrocosmic child [26]. Prevalence of GDM ranged from 0.3% (95% CI: 0.2 – 0.5) in a descriptive cohort study which used modified O'Sullivan criteria for GDM diagnosis in 2000 [22]to 13.9% (95% CI: 11.5 – 16.4) in high risk women referred for OGTT in a metabolic clinic at a university teaching hospital which used WHO criteria in 2009 [28]. The general trend shows increasing of GDM in Western Africa with time (Figure 3.2).

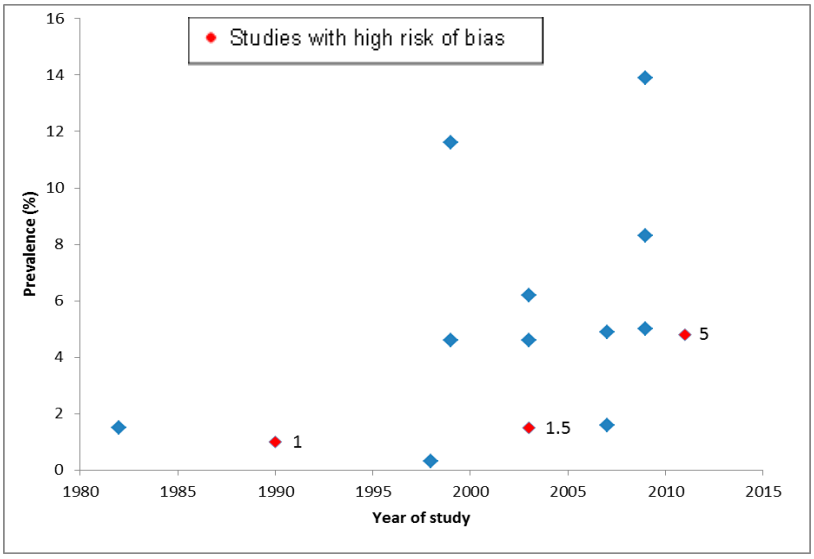

Figure 3.2: Trend of GDM in West Africa: Studies published from 1987 to 2014

South Africa: The earliest study was done in 1969 [32] and the latest in 2010 [33]. The highest prevalence was observed in 1969, a study among Indian women with one or more risk factors (23%,95% CI 18.9-29.2) [32]. With regard to ethnicity, one study was done in a rural Bantu population [34], two in a mixed ethnic population [33, 35], one in subjects from Indian origin [32] and one among combined Indians origin and coloured minority [36]. In this sub- region, a general trend could not be

clearly seen from the plot (Figure 3.3), likely because of the variation in ethnic groups studied.

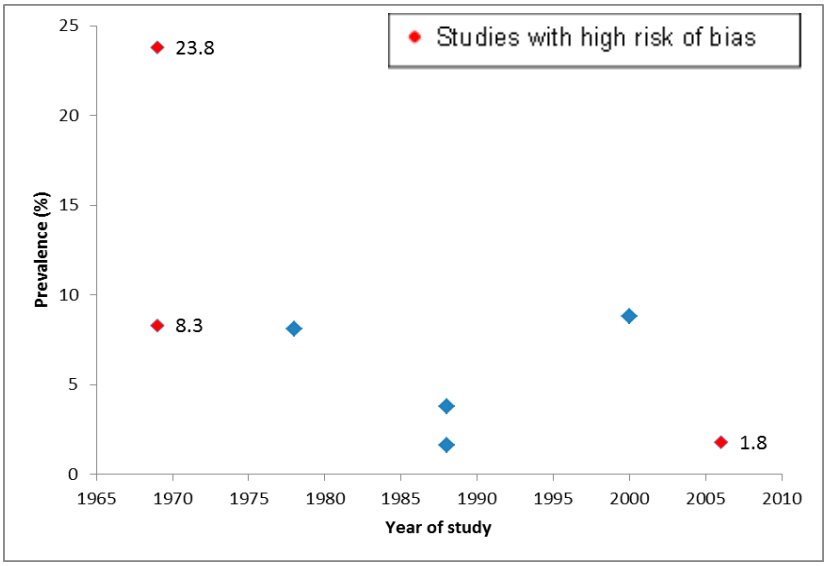

Figure 3.3: Trend of prevalence of GDM for the studies done in South Africa from 1969 to 2010

East and Central Africa: We reviewed six studies from this region; four of them were conducted in East Africa (Tanzania, and Ethiopia) [2, 19, 37, 38] and two in Central Africa (Cameroon and Congo) [39-41]. The oldest study was a community survey in rural Tanzania in 1989 reporting no existence of GDM in the study population (0%) [37], and the most recent study was published in 2014 on rural and urban clinics in Tanzania reporting a prevalence of 1% (95% CI: 0.2-2.9) and 8.4% (95% CI 6.3-10.9) respectively, using WHO diagnostic criteria [2]. Almost all the studies in East and Central Africa used WHO criteria except the study in Cameroon where American Diabetes Association (ADA) criteria was used and a cohort study in Congo where the authors reported using WHO criteria for diagnosis of GDM but blood glucose was measured fasting only. Studies done in early nineties showed low prevalence specifically compared to the studies done after 2010 (Figure 3.4).

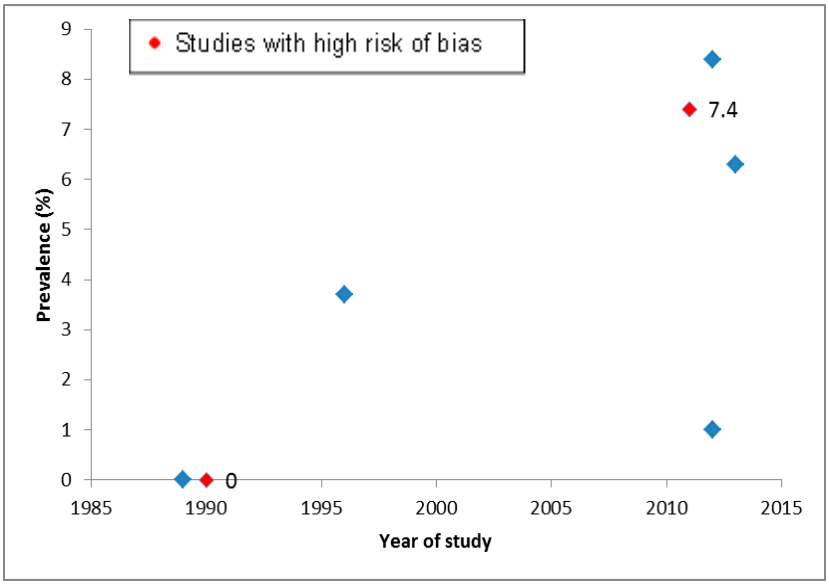

Figure 3.4: Trend of GDM in East and Central: studies published from 1991 to 2014

Screening practices and diagnosis criteria

In most studies, screening was done at gestational age of ≥ 24 weeks. Except of one Tanzanian study, which excluded teenagers, other studies assessed women attending ANC regardless of their age using either universal or selective screening based on risk factors. The commonly used diagnosis criteria were WHO 1985/1999, reported in 13 studies, two studies used ADA criteria (either 2002 or 2010) and older ones applied NDDG (1979) or O'Sullivan criteria (1964), own local criteria or a combination of methods (Table 3.1). Thus, there were differences in screening and diagnosis criteria used even among studies done within the same country and same period. Two studies compared two diagnosis criteria, WHO and NDDG/ EASD, where more women were diagnosed using WHO as compared to other two criteria: 11.6% (95% CI 7.0-17.8) vs 4.6% (95% CI 1.7-9.8) in Nigeria [23] and 3.8 (95%CI 6.0-10.5) vs 1.6% (95% CI 1.0-2.2) in South Africa [36].

Sources of heterogeneity

As indicated in the methods, only studies judged as having low or moderate risk of bias were included in the meta-regression. The meta-regression analysis showed high heterogeneity among the reviewed studies (I^2 = 100, p < 0.001), hence results could not be reliably pooled. None of the study characteristics were significantly associated with the prevalence (Table 3.2) and in all models the heterogeneity remained high (I^2 =100%, p< 0.001). Mutual adjustment in meta-regression was not possible due to limited power.

Table 3.2: Prevalence estimates according to selected study characteristics

			95% CI		
Variable		**Prevalence (%)**	**Lower**	**Upper**	**P- value***
Study setting	Rural	3.52	1.80	5.76	0.59
	Urban	4.59	2.54	7.18	
Diagnostic criteria^	Old criteria^	4.25	2.58	6.30	0.39
	Recent criteria^^	5.11	2.27	8.95	
Population studied	less risk	3.76	2.26	5.60	0.21
	high risk	6.52	2.01	13.24	
Year the study was completed	< year 2000	3.17	2.15	4.37	0.37
	≥ year 2000	5.06	1.68	10.01	
Study sub-region	West Africa	4.90	1.44	10.10	0.40
	South Africa	3.92	2.23	6.04	
	East and Central Africa	3.25	1.27	6.03	

*P-value derived from meta-regression of prevalence on study characteristic.

^ O'Sullivan, NDDG, WHO 1985 and own

^^ ADA 2002, 2010, WHO 1999 and EASD

Risk factors associated with GDM

Associations with potential risk factors for GDM were reported in six studies; four from Nigeria [25, 27, 28, 30], one from Cameroon [40] and one from Tanzania [2]. The commonly reported risk factors were overweight or obesity classified using MUAC, BMI, or body weight, family history of diabetes, previous unexplained stillbirth, previous foetal macrosomia and age ≥30 years. Polyhydramnios and current glycosuria were reported to be associated with GDM in only one study (Table 3.3). In four studies, assessed associations were not adjusted for confounders.

Table 3.3: Risk factors associated with GDM as reported in the reviewed studies done in SSA published between 1969 and 2014

Risk factors	Study	OR (CI)	Comments
MUAC ≥28cm	Mwanri *et al.* (2014)	1.9 (1.1 – 3.3)	Adjusted for previous still birth, family history of diabetes, haemoglobin level
BMI ≥ 25	Fawole *et al.* (2014)	2.3 (1.0 - 5.1)	Unadjusted OR
Obesity (>90 kg)	Anzaku & Musa (2013)	NR	Significantly associated with higher likelihood of GDM (Univariate)*
Family history of Type 2 diabetes mellitus	Mwanri *et al* Mwanri *et al*. (2014)	2.1 (1.1 – 4.2)	Adjusted for previous still birth, MUAC and haemoglobin level
	Kuti *et al*. (2011)	NR	Independent association using multiple regression model
Previous GDM	Kuti *et al.* (2011)	NR	Independent association using multiple regression model
	Fawole *et al.* (2014)	123.7 (58.2-263.2)	Unadjusted OR
Previous/unexplained still birth	Fawole *et al.* (2014)	3.1(1.2-8.5)	Unadjusted OR
	Mwanri *et al*. (2014)	2.8 (1.5 – 5.4)	Adjusted for MUAC, family history of diabetes, haemoglobin level
Previous foetal macrosomia	Fawole *et al.* (2014)	3.9 (1.5-10.7)	Unadjusted OR
	Fawole *et al.* (2014)	3.25 (1.0-10.5)	Adjusted for stillbirth, BMI, family history for type 2 diabetes
	Anzaku & Musa (2013)	11.1 (2.9-42.1)	Adjusted for age, obesity, polyhydramnios, current glycosuria
Age categories (≥35 years)	(Ewenighi *et al*. 2013)	NR	Significant using Chi-square test in three age categories
Age ≥31 years	Anzaku & Musa (2013)	NR	Significantly associated with higher likelihood of GDM (Univariate)*

	Kuti *et al.* (2011)		Independent association using multiple regression model
Age ≥30 years	Jao *et al*. (2013)	NR	Adjusted for gestational age, family history of diabetes mellitus, HIV and pre-pregnancy BMI
Polyhydramnios	Anzaku & Musa (2013)	NR	Significantly associated with higher likelihood of GDM (Univariate)*
Current glycosuria	(Anzaku & Musa (2013)	NR	Significantly associated with higher likelihood of GDM (Univariate)*

* Significant in univariate analysis using chi-square or fisher tests; NR: not reported
MUAC: mid upper arm circumference; OR: Odds Ratio; BMI: Body Mass Index

Discussion

Prevalence and trend of GDM

We systematically reviewed existing literature to assess the prevalence of GDM and its associated risk factors in SSA. We identified 22 studies conducted in six out of the 47 SSA countries; half of the studies (eleven studies) were from West Africa, specifically Nigeria. We observed higher prevalence proportions, although not significantly so, when selective screening for only high-risk women was done compared to universal screening, when studies were more recent, or when more recent diagnostic criteria were used.

Regardless of diagnostic criteria and study setting, we generally observed that the prevalence of GDM in SSA is in a range comparable to the 2 to 6% as reported for European countries [42], and even higher prevalence proportions were observed after selective screening. Our graphs also indicate that the prevalence of GDM increased with time. Similar results were reported in some Asian countries [43], where the evidence of increased in trend was noted in China. The observed increase in prevalence of GDM with time is likely to be due to changes in lifestyle associated with urbanization, including dietary changes and sedentary lifestyle, which lead to overweight and obesity. Obesity is rising in SSA as well [44]; and specifically, in Africa, it has been shown that obesity is more prevalent in women than in men [45]. Another factor could be that women are becoming pregnant at more advanced age, which has recently been reported for SSA as well [46, 47].

Different screening and diagnostic criteria were used and individual studies which compared different diagnostic criteria found that there were significant difference in prevalence when different criteria were used [23, 36]. Variation in methods for screening and diagnosis of GDM was also reported among other European and Asian countries [42, 43]. However, our meta-regression analysis did not show statistically significant associations of diagnostic criteria with the prevalence of GDM.

More studies were conducted in urban compared to rural areas, but the meta-regression analysis did not show any influence of study setting on the prevalence of GDM. This may be in contrast to results from India, where higher prevalence proportions in urban compared to rural populations were reported [48, 49]. On the other hand, in Nigeria and Ethiopia prevalence proportions in rural populations were similar to those reported for urban communities[30, 34, 38]. This may be due to differences in diagnosis criteria used or other factors, such intrauterine exposure of the studied population to undernutrition which is an additional risk factor for GDM [50, 51].

Risk factors

The reported risk factors in our review were advanced maternal age, overweight and obesity, previous macrosomia, previous still birth, family history of Type 2 diabetes mellitus, history of GDM in the previous pregnancies, polyhydramnios and glycosuria [2, 25, 27, 28, 30, 40]. This is similar to results of studies in other regions which reported advanced maternal age (>30 years), BMI and history of GDM as risk factors for GDM [52]. However, three of our reviewed studies did not find a significant association between GDM and family history of Type 2 diabetes [25, 30]. Undiagnosed diabetes is highest in SSA [1]; hence the family history for type 2 diabetes might not be known to many people, thus underestimating the frequency of a positive family history.

Three reviewed studies identified overweight or obesity as a risk for GDM, but all used different classifications. Of the two Nigerian studies, one used BMI cut off of ≥25 kg/m^2[27] and the other one used weight of > 90kg [25]. A study in Tanzania used MUAC ≥28 cm [2]. In SSA setting, weigh measurements is not regularly done so it is difficult to estimate pre-pregnancy weight accurately from maternal recall. Another possible estimation would be BMI during first visit [53], but this is hampered by late initiation of antenatal clinic visits. There is a need for further studies to establish BMI cut offs during pregnancy and to better classify obese and overweight women during pregnancy in SSA.

Several studies in our review included selective screening based on risk factors, and reported that it was a common practice in e.g. Nigeria [22, 26, 28] and South Africa [33]. However, the criteria for identifying women at risk were different, even in studies done within the same country. Higher GDM prevalence in women with at least one risk factor compared to the general population implies that selective screening and or counselling of a high-risk group could be a better option in SSA as there are limited resources. However, if selective screening is to be used, there is a need for establishing simple, suitable and acceptable criteria for identifying women at risk in the SSA setting.

Limitations

This review presents up to date information on the prevalence and risk factors for GDM in SSA. Nevertheless, it is important to mention some limitations. Although most studies excluded known diabetes patients, due to the high prevalence of undiagnosed type 2 diabetes mellitus in the African population some women diagnosed as having GDM might have had type 2 diabetes mellitus, which was undiagnosed until when they were pregnant. In addition, very few studies indicated to have tested the women after delivery to investigate disappearance of GDM. In a rural Ethiopian study, among the 33 women diagnosed with GDM 15 (45%) had blood glucose levels in the diabetes range, 4 to 6 weeks postpartum, which shows that they might have had undiagnosed diabetes [38]. Hence, the true prevalence of GDM in SSA was probably overestimated. All reviewed studies were from six out of 47 SSA countries, and half of them (50%) were from only one West African country, Nigeria. Hence, it is difficult to draw conclusion regarding the prevalence and risk factors for GDM in all SSA countries. In addition, we included studies done in different ethnic groups other than African. Gestational diabetes was noted to vary according to ethnicity and/or racial differences where some ethnic or racial groups were relatively at higher risk compared to others irrespective of their BMI [54]. However, this does not affect our conclusion.

Conclusion

There are few studies on prevalence and risk factors for GDM in SSA. The heterogeneity of the reviewed studies was high, and could not easily be explained by selected study characteristics. The prevalence was as high as about 14% when women with at list one risk factor were studied, which indicates that preventive actions should be taken to reduce the short and long term complications related to GDM in SSA.

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Appendix 3.1: Search terms used for final search 20th June 2014				
Search	**Add to builder**	**Query**	**Items found**	**Time**
#9	Add	Search ((((((((((((diabet* OR hyperglycemi* OR glucose intolerance OR gestational diabetes OR impaired glucose tolerance OR diabetes mellitus OR postprandial glucose tolerance)) OR glucose tolerance)) AND (((pregnan*) OR gestation*) OR Gravid*))) OR gestational diabetes)) AND ((Africa* OR East Africa* OR North Africa* OR Central Africa* OR Angola* OR Benin* OR Botswan* OR Burkina Faso OR Burkinabe* OR Burundi OR Cameroon* OR Cape Verde* OR "Central African Republic" OR Chad* OR Comor* OR Congo* OR Cote d'Ivoire OR Ivory Coast OR Ivorian OR Djibouti* OR Dominica* OR Ecuador* OR Guinea* OR Eritrea* OR Ethiopia* OR Gabon* OR Gambia* OR Ghana* OR Kenya* OR Lesotho OR Liberia* OR Madagasca* OR Malawi* OR Mali* OR Mauritania* OR Mauritius OR Mozambi* OR Namibia* OR Niger* OR Rwanda* OR Senegal* OR Seychell* OR Sierra Leone* OR Somali* OR South Africa* OR Sudan* OR Swaziland OR Swazi OR Tanzania* OR Togo* OR Tonga* OR Uganda* OR Zambia* OR Zimbabwe*)))))) AND Human) NOT animal)	1064	02:29:4

Appendix 3.2: Characteristics of studies that were excluded after full screening of the article

Author (Year of publication)	Title	Reason for exclusion
Macaulay et al (2014)	Gestational diabetes mellitus in Africa: A systematic review	Review
Jiwani et al (2012)	Gestational diabetes mellitus: results from a survey of country prevalence and practices	Worldwide survey, experts opinion regarding prevalence, screening and management of GDM
Hall et al (2011)	Diabetes in Sub Saharan Africa 1999-2011: epidemiology and public health implications. A systematic review	Review
Cpyrky et al (2008)	Gestational diabetes mellitus - an analysis of risk factors	Out of the region (Poland)
Challis et al (2002)	Gestational diabetes mellitus and foetal death in Mozambique: an incident case-referent study	checked after delivery or child loss hence does not fit in to GD definition
Van Bogaert (1998)	Gestational diabetes mellitus--are African diagnostic criteria warranted?	Diagnosis criteria
Kinnear and Ojo (1966)	Pregnancy and diabetes in Nigeria	Already known Type 2 diabetic women
Hailu and Kabede (1994)	High-risk pregnancies in urban and rural communities in central part of Ethiopia	Assessed risk factors associated with poor birth outcome but GDM was not assessed.
Iloki et al (1993)	Diabetes and pregnancy in Africa: a pathology often not recognized	Most information is missing
Iloki et al (1992)	Diabetes and pregnancy in Africa. An often overlooked pathology	Same data and content as Iloki 1993
Fraser (1981)	The effect of pregnancy on the normal range of the oral glucose tolerance in Africans	Compared blood glucose range in normal and pregnant women

Notelovitz (1974)	Gestational diabetes in general practice	Not relevant, discussed the role of health practitioner
Notelovitz (1970)	Diabetes screening during pregnancy	Screening criteria
Notelovitz (1970)	The pregnant Bantu diabetic	Not enough information to establish prevalence
Notelevitz (1969).	The pregnant Natal Indian diabetic	Description of Indian diabetic pregnant women
Notelovitz (1968)	The pregnant Natal Indian diabetic-facts and fancies	repeated results in another published paper by the same author

Appendix 3.3: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	

Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression (see Item 16)).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

Appendix 3.4a: Risk of bias assessment tool: Adapted from the Risk of Bias Tool for Prevalence Studies developed by Hoy, Brooks, Woolfe et al. (2012)

Name of the author and year of publication.....

Risk of Bias Item	**Answer: Yes (Low Risk) or No (High risk)**
External Validity	
1. Was the study target population a close representation of the national pregnant population in relation to relevant variables?	
2. Was the sampling frame a true or close representation of the target population? **(risk factors used appropriate?)**	
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	
4. Was the likelihood of non-participation bias minimal? **(i.e. ≥75% response rate)?**	
Internal Validity	
5. Were data collected directly from the subjects? (as opposed to medical records)	
6. Were acceptable diagnostic criteria for GDM used?	
7. Was a reliable and accepted method of testing for blood glucose utilised?	
8. Was the same mode of data collection used for all subjects?	
9. Was GDM tested for within the advised gestational period of 24-28 weeks?	
10. Were the numerator(s) and denominator(s) for the calculation of the prevalence of GDM appropriate?	
11. Summary item on the overall risk of study bias LOW RISK OF BIAS: 8 or more "yes" answers. Further research is very unlikely to change our confidence in the estimate. MODERATE RISK OF BIAS: 6 to 7 "yes" answers. Further research is likely to have an important impact on our confidence in the estimate and may change the estimate. HIGH RISK OF BIAS: 5 or fewer "yes" answers. Further research is very likely to have an important impact on our confidence in the estimate and is likely to change the estimate.	

Appendix 3.4b: Assessment of risk of bias of the included studies

Author (year of publication)	Were the sampled pregnant women representative?	Was sampling frame representative?	Random or census selection?	Response rate ≥75%?	Data from subjects?	Acceptable diagnostic criteria?	Reliable testing for BG?	Same method for all?	Was GDM testing time proper?	Proper calculation of prevalence	Total "Yes"	Overall risk of bias
Abudu and Kuti 1987	No	yes	yes	yes	yes	no	yes	yes	yes	yes	8	Low
Wokoma et al 2001	No	yes	yes	NS	yes	no	no	yes	yes	yes	6	Moderate
Ozumba et al 2004	No	no	no	yes	no	yes	yes	yes	no	yes	5	High
Olarinoye et al 2004	No	yes	yes	yes	yes	yes	yes	yes	no	yes	8	Low
Adegbola et al 2008	No	yes	no	yes	yes	yes	yes	yes	yes	yes	8	Low
Kamanu et al 2009	No	no	no	yes	no	yes	no	yes	NS	no	3	High
Kuti et al 2011	No	no	yes	NS	yes	yes	yes	yes	yes	yes	7	moderate
Ugboma et al 2012	Yes	yes	no	no	yes	yes	no	no	no	yes	5	High
Ewenighi et al 2013	No	yes	yes	yes	yes	yes	yes	yes	no	yes	8	Low
Anzaku et al 2013	No	yes	yes	yes	yes	yes	yes	yes	yes	yes	9	Low
Fawole et al 2014	No	yes	yes	yes	no	yes	yes	no	no	yes	6	moderate
Notelovitz 1969	No	yes	NS	NS	yes	yes	yes	yes	no	no	5	High
Jackson and Coetzee 1979	No	yes	yes	NS	yes	yes	yes	yes	yes	no	7	Medium

Ranchold et al 1991	No	yes	yes	NS	yes	yes	yes	yes	yes	yes	8	Low
Mamabolo et al 2007	No	no	ye	ye	yes	yes	yes	yes	no	yes	7	moderate
Basu et al 2010	No	no	yes	NS	no	no	NS	yes	NS	Yes	3	High
Jao et al 2013	No	yes	yes	NS	yes	yes	yes	yes	yes	yes	8	Low
Mwanri et al 2014	Yes	yes	yes	yes	yes	yes	no	yes	no	yes	8	Low
Swai et al 1991	Yes	yes	yes	yes	yes	yes	yes	yes	no	yes	9	Low
Lutate et al 1993	No	no	no	no	yes	yes	NS	yes	no	yes	3	High
Seyoum et al 1999	No	yes	yes	yes	yes	yes	yes	yes	yes	yes	9	Low
Tandu-Umba et al 2013	No	no	no	NS	yes	no	yes	yes	yes	yes	5	High

Chapter 4

High blood pressure and associated risk factors among women attending antenatal clinics in Tanzania

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Abstract

Aim: Hypertensive disorders of pregnancy (HDP) is one of the leading causes of maternal and perinatal mortality worldwide. This study examined prevalence and potential risk factors for HDP among pregnant women in Tanzania.

Methods: We examined 910 pregnant women, age ≥20 year, mean gestational age 27 weeks, from rural (n=301) and urban (n=609) areas during their usual antenatal clinic visits. Hypertension was defined as clinic SBP ≥140 mmHg or DBP ≥90 mmHg. Dietary assessment included dietary diversity score (DDS) using 16 food groups. Multiple logistic regression analysis was used to assess the independent association of risk factors associated with prevalence of hypertension.

Results: Hypertension was observed in 70 women (7.7%). After excluding the 8 women who were already on management, 62 women (6.9%) had HDP, prevalence being higher in urban (8.1%) compared to rural area (4.4%). For the urban area, mother's age (OR 1.10; 95% CI 1.03 – 1.20), gestational age (OR 1.10; 95% CI 1.02-1.20), mid-upper arm circumference (MUAC) (OR 1.13; 95% CI: 1.01-1.23), DDS (OR 1.31; 95%CI 1.20-1.60) and being HIV positive (OR 2.40; 95% CI 1.10-5.18) were independently associated with HDP. When adjusted for proteinuria, associations with HIV status and MUAC weakened. In the rural area, HDP risk increased with age and gestational age.

Conclusion: Prevalence of HDP was higher in urban compared to rural area, which points at high risk for preterm delivery, low birth weight and future cardiovascular diseases. The observed risk factors identify risk groups to be screened and targeted for prevention. The role of HIV status needs to be further explored.

Introduction

Hypertensive disorders are the most common medical problems in pregnancy and account for about 10% of maternal deaths worldwide. They affect women in every region, causing 9% of maternal deaths in Africa and Asia, over 16% in industrialized countries and more than 25% in Latin America and the Caribbean [1]. Hypertension during pregnancy is usually thought of as a short term problem that resolves itself after delivery but still carries significant risk to the mother such as risk of recurrence, cardiovascular complications, stroke and renal disease [2, 3]. It has also been associated with elevated risk of preterm birth, low birth weight and low Apgar score [4]. It is estimated that approximately 30% of hypertensive disorders of pregnancy (HDP) are due to chronic hypertension and 70% are due to gestational hypertension [5]. However, due to low screening and poor health seeking behaviour in Tanzania, it is likely that the majority of the pregnant women do not know their hypertension status before pregnancy.
Risk or predisposing factors for HDP include older maternal age (above 30 years), multiple pregnancy, diabetes, obesity, family history of preeclampsia and excessive weight before or during pregnancy [6-9]. Rural residence, low socioeconomic status, urinary tract infection, inter-pregnancy spacing and stress were also reported as risk factors [6]. In addition, hypertension was associated with placental malaria infection and non-proteinuric hypertension in women living in malaria-hypo endemic area [10]. However, risk factors for HDP may differ among various ethnic groups and by degree of prenatal care [8, 11]. Although Antenatal clinic (ANC) attendance in Tanzania is generally high (96%), only about two third (68%) of the pregnant women had their blood pressure measured and about half (52%) had their urine collected [12]. There is limited information on HDP and possible attributable factors in Tanzania.

Like HDP, prevalence of gestational diabetes mellitus (GDM) is increasing worldwide [13] and it is also becoming a public health concern in Sub Saharan African countries where prevalence was reported to vary across the region and have been increasing in the past decade [14, 15]. Some studies suggest that gestational diabetes, glucose intolerance and insulin resistance have a role in HDP [16,17]. Nevertheless, few studies in Sub Saharan Africa explored association of blood glucose level and HDP in an African population.

This study aimed at assessing the prevalence of HDP among rural and urban women attending ANC in randomly selected centres and to determine the

association between GDM and other factors with HDP. The results will help in the surveillance and management of mothers at risk and hence reduce maternal and child morbidity and mortality associated with HDP.

Methods

Study design and setting

A cross sectional study was conducted from August 2011 through May 2012 in selected health facilities in Morogoro and Dar es Salaam regions. The study population was women attending ANC in two selected health facilities from each of the three districts in Dar es Salaam region and two health facilities in Kilombero district, Morogoro region. A total of 910 women, at gestational age of 20 to 36 weeks were assessed during ANC visits. Women with serious medical conditions, those with known type 1 or type 2 diabetes mellitus, those who were hospitalised and women who could not tolerate oral glucose tolerance test (OGTT) were excluded. In assessing the risk factors, we also excluded eight women who were hypertensive before pregnant since they might have changed their lifestyle hence modified risk factors.

Data collection

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was measured from mid-upper-arm of the left side while the respondent was sitting and relaxed for 10 minutes before the actual measurement, using a digital blood pressure (BP) device (Microlife BPA100, Widnau, Switzerland) which was validated [18]. Two BP measurements were done within an interval of five to ten minutes. Average systolic and diastolic BP were recorded in mmHg and were used for analysis. Hypertension during pregnancy was defined as SBP of 140 mmHg or higher and DBP of 90 mmHg or higher measured after 20 weeks of gestation in women previously unknown to be hypertensive. Women with HDP were referred to see the doctor for further investigation and treatment.

Women were requested to collect midstream urine on the spot in a provided sterilized disposable plastic container. Urine samples were tested within one hour for glucose, ketones, leucocytes and protein using dipstick made with a color sensitive pads (urine strip 10 C, Dialeb GmbH, Austria). Women were considered with proteinuria when the dipstick was +1 or more in the absence of urinary tract infection [19].

Blood glucose was measured in capillary blood at fasting state and at two hours after 75 gram oral glucose tolerance test using HemoCue Glucose B-201

(Ängelholm AB, Sweden) and recorded in mmol/L during the usual visit for ANC. Diagnosis of GDM was based on WHO criteria [15].

Haemoglobin (Hb) concentrations were measured using HemoCueHb 201+ Haemoglobin photometer (HemoCue AB, Ängelholm, Sweden) and recorded to the nearest 0.1 g/dl. Women were classified as having severe (<7 g/dl), moderate (7 to 9.9 g/dl), mild (10 to 10.9 g/dl) anemia or having normal Hb (≥11 g/dl).

Dietary assessment was done using a validated dietary diversity questionnaire [20]. Respondents were asked to recall all the foods consumed in the previous 24 hours immediately prior to the survey. They were prompted to include all snacks and foods eaten outside home and details of the ingredients added to each food were noted. Consumption of a particular group scored 1, and if a group was not consumed a score of 0 was given. Dietary diversity score (DDS), an indicator of nutrient adequacy and a proxy measure of nutritional quality of an individual's diet[21, 22], was defined as a total count of different food groups consumed in the past 24 hours without considering the amount or portion size. Number of food groups used in dietary diversity can vary according to the study objective, and currently there is no internationally recommended food group list to be included in the score at individual level for different age/sex groups [20]. We used the questionnaire with 16 food groups to capture micronutrients intake as well as consumption of sweets and beverages which are known to be associated with metabolic syndrome. All foods consumed were categorized in one of the 16 food groups depending on the nutrient composition in the food composition table [23]. The food groups included cereals; white roots and tubers; vitamin A rich vegetables and tubers; dark green leafy vegetables; other vegetables; vitamin A rich fruits; other fruits; organ meat; flesh meat; eggs; legume, nuts and seeds; fish and sea foods; milk and milk products; oil and fats; sweets; spices, condiments and beverages. DDS was divided into three categories and classified as low (0 to 5), medium (6 to 8) and high (9 to 16).

Women were interviewed about their age, marital status, education level, occupation and family history of diabetes using a pre-tested structured questionnaire. Information on current pregnancy, gestational age, parity and HIV status was obtained from ANC card and or interviews. Multipara mothers were asked to recall age of the previous last child and this was verified through growth monitoring card during the next visit. The information on age of the previous child or years after the last pregnancy was used to estimate child spacing or inter-

pregnancy duration. Gestational age was estimated using the first date of last normal menstrual period which is the commonly used method in most antenatal clinics in Tanzania, and ultrasound was not done.

Physical activity was assessed retrospectively by using the short form of the International Physical Activity Questionnaire (IPAQ) which was translated into Kiswahili. The IPAQ short form is designed and tested for adults aged 15 to 69 years [24] The IPAQ short form assess specific types of activity such as walking, moderate intensity activities and vigorous intensity activities. Women were asked to recall their activities from the day of the interview up to seven days backward. Data was reported as metabolic equivalents (MET-minutes per week) according to IPAQ scoring protocol which categorized women into high, moderate and low METS groups [25].

Anthropometric measurements were taken during antenatal visit. Weight of the mothers (in kg) was measured using Seca electronic scale (SecaGmbh and Co.kg 22061, Hamburg, German). Height (in cm) was measured without shoes using height measuring board (Shorr productions, Maryland USA). Weight was recorded as for the first visit for women whose visit to ANC was the first during that pregnant and those who had previous visit, weight during first visit was retrieved from ANC card and used to calculate BMI at booking. Mid-upper-arm circumference (MUAC) was measured using non-stretching MUAC tape and recorded to the nearest cm. Like other developing countries, most Tanzanian women could not recall their pre-pregnancy weight. Additionally, weight gain monitoring is not possible due to limitations of facilities and staff and due to late start of ANC visits [12]. MUAC was therefore used as a proxy for pre-pregnancy BMI. MUAC is known to be relatively stable during the course of pregnancy and was highly correlated with pre-pregnancy BMI in a previous study [26]. MUAC was further divided into quartiles which were numbered sequentially from Q1 (the group with lowest MUAC values ≤24.5 cm) to Q4 which was the group with highest MUAC values (≥29.0 cm).

Ethical consideration

The protocol of this study was approved by Tanzania National Institute of Medical Research and the respective District Authorities. The participants were informed about the study, its objectives, expected outcomes, benefits and risks for their participation, and ensured confidentiality. Informed verbal or written consent was obtained from the participants and in some cases from their partners. All information obtained from the participants was confidential and all who were

identified with any condition requiring medical attention were referred to medical doctor in charge of the reproductive and child health clinic for further assessment and treatment.

Data Analysis

Data were entered, cleaned and analysed using IBM SPSS Statistics version 19. Maternal socio-demographic characteristics and biosocial data were compared between those living in rural and urban areas. In addition to descriptive analysis, categorical variables were compared using Chi-Square test while comparison of means was done using Student's t-test. Univariate analysis was done to identify variables associated with presence of HDP. Crude odds ratio (OR) and OR adjusted for age, gestational age and/or MUAC were calculated. Multiple logistic regression analysis was done to assess independent association of selected variables with HDP. All variables with p-value of ≤0.125 in the univariate analysis were entered in the model and analysed using backward elimination. Presence of proteinuria was included in a second multiple regression model. Data were stratified according to residence. In the analyses age, gestational age, number of years since last pregnancy, MUAC and DDS were treated as continuous variables.

Results

Majority of the studied women were married (83%), and less than a quarter (23%) had secondary education or higher. Pregnant women in the rural area were younger, had more number of children, higher mean gestational age at first visit and lower BMI at booking (Table 4.1). The mean SBP was 111 mmHg (95% CI: 109.8 – 112.5) vs 114.6 mmHg (95% CI: 113.6 -116.0) in rural compared to urban women; DBP was 70.2 mmHg (95% CI: 69.3-71.5) vs 72.4 mmHg (95% CI: 71.6-73.4). Mean DDS in urban women (6.7; 95% CI 6.6-6.9) was significantly higher than in rural women (6.4; 95% CI:6.3-6.6), whereas mean MUAC and gestational age were similar in both groups. Twelve women (4.0%) in rural area and 59 women (9.8%) in the urban area were HIV positive. About two out of five women in the rural area and one out of five women in the urban had high physical activity level. Alcohol drinking was more common in the urban (12%) compared to rural area (8%). Smoking is uncommon for Tanzania women, only seven women reported to smoke and they were all from the urban area

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Table 4.1: Characteristics of the studied women in urban and rural areas (2011/2012 survey, Tanzania)

Characteristic	Rural (n=298) Mean	95%-CI	Urban (n=604) Mean	95%-CI	P-value
Age (years)	26.6	26.0 - 27.2	27.5	27.1 - 28.0	0.016
Current gestational age (weeks)	28.1	27.6 - 28.8	28.1	27.7 - 28.5	0.770
1st visit Gestational age (weeks)	21.0	20.0 - 21.0	18.0	17.6 - 18.3	0.000
Parity	2.6	2.4 - 2.8	2.4	2.5 - 2.5	0.046
MUAC (cm)	27.1	26.7 - 27.5	27.2	26.5 - 27.6	0.463
BMI (Kg/m^2)	26.1	25.6 - 26.5	26.7	26.3 - 27.0	0.045
Systolic blood pressure (mmHg)	111.0	109.8 - 112.4	114.6	113.6 - 116.0	0.000
Diastolic blood pressure (mmHg)	70.3	69.3 - 71.5	72.4	71.6 - 73.4	0.007
Haemoglobin level (mg/dl)	9.9	9.7 – 10.1	10.1	9.9 – 10.2	0.130
Fasting blood glucose (mmol/L)	4.0	3.9 - 4.1	4.6	4.5 - 4.7	0.000
2-hr blood glucose (mmol/L)	5.1	4.9 - 5.2	6.1	5.9 - 6.2	0.000
DDS16	6.4	6.3 - 6.6	6.7	6.6 - 6.9	0.006
	n	**%**	**N**	**%**	
Marital status					
Married	277	93.0	539	89.2	0.074
Single	21	7.0	65	10.8	
Education level					
Informal	43	14.4	36	6.0	
Primary	197	66.1	418	69.2	0.000
Secondary and post-secondary	58	19.5	150	24.8	
Occupation					
House work	87	29.2	292	48.3	
Formal employment	25	8.4	1.2	16.9	0.000
Petty business	87	29.2	207	34.3	
Agriculture	99	33.2	3	0.5	
DDS					
Low	75	25.2	122	20.2	
Medium	202	67.8	400	66.2	0.008
High	21	7.0	82	13.6	
METS					
Low	35	22.3	122	28.1	
Medium	137	30.5	312	51.7	0.000
High	126	42.6	170	20.2	
HIV Positive	12	4.0	59	9.8	0.003
Proteinuria	2	0.7	67	11.1	0.000
Alcohol drinking (yes)	23	7.7	74	12.3	0.039

Values for continuous data are Mean (95% CI of the mean), categorical data are n (%), P values are from t-test and Chi-square test

Prevalence of HDP was 7.7% (95% CI 6.0 – 9.4). After excluding the 8 women who were already on management and hence probably modified their risks, 62 women (6.9%; 95%CI; 5.2 – 8.5) had HDP, the prevalence being higher in the urban (8.1%; 95% CI: 6.8 – 11.4) compared to the rural area (4.4%; 95% CI: 2.1 – 6.7) (Table 4.2).

The mean SBP for the hypertensive group was 146.6 (SD 16.9) mmHg and ranged from 140 to 189 mmHg; mean DBP was 97.7 (SD 10.0) mmHg and ranged from 90 to 126 mmHg. Among women with HDP 23 (37.1%) had proteinuria while among women with normal BP 46 (5.5%) had proteinuria. In univariate analysis, women with five or more previous pregnancies, a pregnancy more than 10 years since the last pregnancy, more than 30 weeks of gestation and those with previous still birth were more likely to have HDP. Likewise, there was higher prevalence of HDP in women with MUAC in the highest quartile compared to those in the lowest quartile (14% vs 4.6%), in HIV positive compared to those without HIV (14.1% vs 6.3%), with proteinuria compared to those without (33% vs 4.7%) and in those with high DDS (13.6%) compared to those with medium (7%) or low DDS (3%). When adjusted for age and gestational age, only area of residence, MUAC, proteinuria and DDS remained significant. Other factors such as familial history of type 2 diabetes mellitus, GDM, Hb level, physical activity, occupation and education were not significantly associated with hypertension. Although the rural and urban difference was reduced when adjusting for age and gestational age, the difference persisted even after adjusting for other education, marital status, occupation, parity, MUAC and HIV status (OR 2.01; 95%CI 1.03-3.94). Proteinuria was present in 18.3% of HIV infected women compared to 6.7% in uninfected women (P<0.001).

Table 4.2: Comparison of selected socio-economic, obstetric and biochemical risk factors among women with and without HDP (ANC survey 2011/2012)

Characteristic	NBP		HDP			
	n	%	n	%	Crude OR (CI)	Adjusted OR (CI)
Residence						
Rural	285	95.6	13	4.4	1	1
Urban	555	91.9	49	8.1	1.94 (1.03 – 3.63)	1.90 (1.1 – 3.6)
Age*						
≤ 24 years	305	95.6	14	4.4	1	1
25 to 29 years	296	95.8	13	4.2	0.96 (0.44 – 2.07)	0.84 (0.38 – 1.82)
30 to 34 years	165	93.8	11	6.2	1.45 (0.65 – 3.27)	1.10 (0.47 – 2.55)
≥ 35 years	74	75.5	24	24.5	7.1 (3.49 – 14.32)	5.32 (2.55 – 11.10)
MUAC						
Q1 (≤ 24.5 cm)	218	95.2	11	4.8	1	1
Q2 (24.5 – 26.9 cm)	206	95.8	9	4.2	0.87 (0.35 – 2.13)	0.72 (0.29 – 2.00)
Q3 (27.0 – 29.0 cm)	228	93.4	11	4.6	0.96 (0.41 – 2.25)	0.83 (0.35 – 2.00)
Q4 (≥ 29.1 cm)	118	85.4	31	14.2	3.27 (1.60 – 6.68)	1.12 (1.1 – 1.7)
Number of previous pregnancies						
First	242	95.7	4	4.3	1	1
2 to 4	539	93.7	36	6.3	1.47 (0.74 – 2.94)	0.92 (0.42 – 2.01)
≥ 5	59	79.7	15	20.3	5.59 (2.44 – 12.81)	1.91 (0.67 – 5.40)
Birth spacing						
< 5 years	312	95.1	16	4.9	1	1
5 to 9 years	168	91.3	16	8.7	1.86 (0.91 – 3.81)	1.43 (0.68 – 3.00)
≥ 10 years	60	83.3	12	16.7	3.9 (1.76 – 8.66)	2.18 (0.94 – 5.12)
Gestational age**						
≤24 weeks	264	96.0	11	4.0	1	1
25 – 29 weeks	255	93.4	16	6.6	1.71 (0.78 – 3.75)	1.7 (0.77 – 3.78)
≥ 30 weeks	351	90.9	35	9.1	2.39 (1.19– 4.80)	2.4 (1.20 – 4.88)
Previous still birth						
No	729	95.7	48	6.2	1	1
Yes	111	88.8	14	11.2	1.92 (1.02 – 3.60)	1.72 (0.90 – 3.30)
History of diabetes						
No	736	93.2	54	6.8	1	1
Yes	104	92.9	8	7.1	1.05 (0.48 – 2.27)	0.98 (0.45 – 2.16)

GDM						
No	789	92.9	60	7.1	1	1
Yes	51	96.2	2	3.8	0.52 (0.12 – 2.17)	0.48 (0.11 – 2.06)
HIV status						
Negative	779	93.7	52	6.3	1	1
Positive	61	85.9	10	14.1	2.46 (1.20 – 5.07)	1.79 (0.85 – 3.80)
Positive +ART	37	88.1	5	11.9	2.02 (0.76 – 5.37)	1.35 (0.49 – 3.68)
Positive newly diagnosed	24	82.8	5	17.2	3.12 (1.14 – 8.51)	2.63 (0.94 – 7.35)
Protein in urine						
Negative	794	95.3	39	4.7	1	1
Positive	46	66.7	23	33.3	10.18 (5.61 – 18.454)	9.62 (5.17 – 17.01)
Hb levels						
<7.0 g/dl	24	85.7	4	14.3	1	1
7.0 – 9.9 g/dl	346	93.3	25	6.7	0.42 (0.13 – 1.29)	0.39 (0.12 – 1.27)
10.0 – 10.9 g/dl	234	92.5	19	7.5	0.39 (0.12 – 1.25)	0.41 (0.12 – 1.38)
≥11.0g/dl	234	91.5	22	8.5	0.48 (0.15 – 1.54)	0.45 (0.14 – 1.49)
Education						
Informal	73	92.4	6	7.6	1	1
Primary	568	92.4	47	7.6	1.10 (0.42 – 2.44)	1.20 (0.48 – 3.00)
Secondary and post-secondary	199	95.7	9	4.3	0.55 (0.20 – 1.60)	0.77(0.26 – 2.33)
Occupation						
House works	350	92.3	29	7.7	1	1
Formal employment	122	96.1	5	3.9	0.50 (0.89 – 1.31)	0.46 (0.17 – 1.23)
Petty business	273	92.6	21	7.9	0.93 (0.52 – 1.66)	0.73 (0.40 – 1.34)
Agriculture	95	93.1	7	6.9	0.90 (0.38 – 2.09)	0.61 (0.25 – 1.50)
DDS						
Low	191	97.0	6		3.01	1
Medium	560	93.0	42	7.0	2.39 (0.99 – 5.71)	2.54 (1.04 – 6.16)
High	89	86.4	14	13.6	5.01 (1.86 – 13.46)	5.84 (2.11 – 16.15)
Physical activities (METS)						
Low	144	91.7	13	8.3		
Medium	418	93.1	31	6.9	0.72 (0.34 - 1.51)	0.82 (0.38 – 1.75)
High	278	93.9	18	6.1	0.82 (0.42 – 1.61)	0.97 (0.48 – 1.93)

NBP, normal blood pressure

*Adjusted for MUAC; **Adjusted OR for age, other variables adjusted for age and gestational age.

In multivariate analysis, in the urban area risk of HDP increased with age of the mother (OR 1.10; 95%CI 1.03 – 1.20), gestational age (OR 1.10; 95%CI 1.10 – 1.20), MUAC (OR 1.13; 95%CI: 1.01–1.23) and DDS (OR 1.31; 95%CI: 1.20–1.61) (Table 4.3). Additionally, those with HIV positive were 2 times more likely to have HDP (OR 2.4; 95% CI 1.10 – 5.18). In the rural area, the risk of HDP increased with the increase in age (OR 1.12; 95%CI 1.00-1.24), gestational age (OR 1.14; 95%CI 1.01 – 1.30) and slightly but not significant with MUAC (OR 1.15; 95%CI 0.99 – 1.35).

Table 4.3: Predictors of hypertension during pregnancy derived from logistic regression with backwards elimination

Characteristic	Adjusted OR	CI	P-value
Urban			
Age (year)	1.10	1.03 – 1.20	0.004
Gestational age (weeks)	1.10	1.02 – 1.20	0.015
MUAC (cm)	1.13	1.01 – 1.23	0.026
DDS	1.31	1.20 – 1.61	0.011
HIV positive	2.40	1.10 – 5.18	0.036
Previous still birth	1.90	0.92 – 3.96	0.085
Rural			
Age (year)	1.12	1.00 – 1.24	0.042
Gestational age (weeks)	1.14	1.01 – 1.30	0.039
MUAC (cm)	1.15	0.99 – 1.35	0.073

When proteinuria was added to the model as a risk factor in the urban area, the results for MUAC, previous stillbirth and HIV status weakened and HIV status and MUAC were not significant anymore (Table 4.4).

Table 4.4: Predictors of hypertension during pregnancy derived from logistic regression after adjusting for proteinuria in urban population

Characteristic	Adjusted OR	CI	P-value
Urban			
Proteinuria	6.94	3.48 – 13.85	0.000
Age (year)	1.10	1.03 – 1.18	0.004
Gestational age (year)	1.08	1.01 – 1.17	0.032
MUAC (cm)	1.07	0.99 – 1.16	0.097
DDS	1.30	1.07 – 1.61	0.014
HIV positive	1.98	0.86 – 4.61	0.111
Previous still birth	1.53	0.70 – 3.36	0.288

Discussion

This study reports prevalence of HDP and associated risk factors among rural and urban Tanzanian women attending ANC. The overall prevalence of HDP (6.9%) was comparable to worldwide estimations of 5 to 10% [7, 27]. Lower prevalence was observed in other studies conducted in Africa [28, 29], as well as in a previous study in rural Tanzania [30]. Much higher occurrence of HDP (32.7%) was reported in South East Nigeria [31]. Rural-urban difference in prevalence of HDP was also reported in Ghana (3.1% in urban vs 0.4% in rural) [28].

The rural-urban differences in HDP observed in this study could partly be explained by high prevalence of HIV in urban compared to rural pregnant women, higher DDS and differences in mean age of the respondents. There are also obvious differences in blood glucose levels, education, occupation and physical activity level among rural and urban women, but none was found to be associated with HDP in this study.

We found that HDP increased with maternal age, even after controlling for MUAC. This is similar to results of studies in other parts of the world [7, 9, 32]. In rural and urban Ghana no association was found between maternal age and BP [28], while in

Cameroon young age was identified as a risk factor for HDP (OR 2.6; 95% CI 1.5–4.7) [33]. In our study teenagers were excluded; however, a higher prevalence of HDP was noted among women above 35 years compared to those below 25 years. In addition, maternal BMI may influence the association between maternal age and the risk of HDP[34]. In our study, also when controlled for age and gestational age MUAC was independently associated with HDP. Several studies reported BMI to be one of the major contributing factors to HDP [8, 28, 31]. The prevalence of obesity among women attending ANC in Tanzania increased from 3.6% in 1995 to 9.1% in 2004 [35]. This means HDP and associated factors may also increase with time if serious preventive action is not taken specifically regarding reducing overweight and obesity before conception.

Women living with HIV had a significantly higher prevalence of HDP (14.1%) compared to their normal counterparts (6.3%) (OR 2.4; 95%CI 1.1–5.2). The prevalence was even higher among the newly diagnosed HIV positive women compared to those who were already on anti-retroviral therapy (ART)**.** A review and meta-analysis on HIV and the risk of direct obstetric complications showed some evidence for increased odds of HDP with HIV infection (OR: 1.46, 95% CI: 1.03–2.05), although with high between study heterogeneity [36]. In the general Sub-Saharan African population [37] and in other studies among HIV infected patients, HIV or ART was not associated with hypertension [38, 39]. However, our data analyses also showed that the presence of proteinuria in HIV positive women may explain this observation, as the association between HIV status and HDP reduced when proteinuria was adjusted for. Proteinuria could be a result of chronic kidney disease which may have resulted from high BP [40, 41]. HIV infection has been associated with both acute kidney injury and chronic kidney disease [42] and studies in Africa reported improvement of kidney function with the use of ART [43, 44], thus could explain higher prevalence of HDP among people who had not started ART compared to these already using ART.

We observed rural-urban differences in mean DDS, and there was 1.3 increased odds of having HDP with increased number of food groups in urban but not in rural women. Although using different number of food groups, studies in Sri Lanka and in Tanzania reported positive associations of DDS with obesity [45, 46]. A study in Teheran found an inverse association between DDS and the risk of high blood pressure, impaired glucose homeostasis and high triglyceride levels [47], but the probability of being obese increased with DDS quartiles [48]. In South Africa, higher mean diastolic blood pressure was observed in the low DDS group [49]. A study in

Mexican men reported that DDS was positively correlated with micronutrient adequacy and fruits and vegetable intake but also with percentage of energy from total and saturated fats and cholesterol intake [50]. The authors concluded that in other settings than those with high prevalence of malnutrition, higher food diversity may not predict a healthier diet.

While most studies reported significant associations between HDP and GDM or insulin resistance [16, 17, 51], we did not find any association between GDM and HDP. Similar results were observed in Bangladesh and in Cameroon [52, 53], where there was no difference between mean SBP and DBP among women with and without gestational diabetes. In a study by Hendriks et al. in the general non-pregnant population in Nigeria, Kenya, Tanzania and Namibia; the association BP and blood glucose levels was only found in Nigerian population [37]. Lack of association between GDM and BP could be due to ethnic differences which needs further exploration since there were only few studies conducted in Africa.

Our study has some limitations. DDS data was collected from a single 24 hour dietary recall to represent usual intake, and counting of food groups does not necessarily consider the amount consumed. Additionally, each food group was given equal weight regardless of its contribution to the risk of hypertension during pregnancy. We assessed physical activity using questionnaire which is more subjective to recall bias, and some women might have changed their activity pattern since they became pregnant.

The assessment of gestational age was based on last menstrual period reported by the mother and thus relies on memory. This might have underestimated or overestimated the actual gestational age especially in the rural area because of low education level and late booking to the ANC. Our study might have been confounded by other factors such as genetics, exposure to pollutants and stress during pregnancy, which were not considered. Blood pressure was estimated from two measurements during a single visit and at the clinic setting, hence the true prevalence might have been overestimated to some extent [54]. However, this is the regular practice in Tanzanian antenal care. Finally, the diagnosis of HDP requires good knowledge on hypertension before pregnancy. We excluded known hypertensives, but due to lack of regular checkups in our African population some of the HDP might have been regular hypertension. Despite of the above limitations, the study still provides necessary information regarding risk factors for HDP in Tanzanian women.

Conclusion

Prevalence of HDP in Tanzania is higher than most of the African countries which signals risks for preterm delivery, low birth weight and future cardiovascular disease. Among the identified risk factors MUAC, which is a proxy for BMI, and DDS were the modifiable risk factors. Interventions to reduce HDP should target overweight and obese women before conception. Moreover, dietary diversity is important regarding micronutrient intake, but in an urban setting it probably also indicates high energy intake, thus further studies are needed specifically on DDS in relation to hypertension among pregnant women. Higher prevalence was also noted among HIV positive women, thus special attention and proper counselling may be provided to this particular group during ANC visits.

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Chapter 5

Maternal risk factors for low birth weight and macrosomia in Tanzania

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Abstract

Aim: Various diseases and health conditions have been shown to be associated with birth weight and delivery complications. This study was undertaken to determine risk factors for macrosomia and low birth weight in a cohort of Tanzanian women.

Methods: A prospective study was conducted in Dar es Salaam city from 2011 through 2012 among 609 pregnant women ≥20 years of age, investigated at mean gestational age 28 weeks for blood glucose levels, blood pressure, anthropometry and socio-demographic data. Information on birth weight, sex of the child, mode of delivery and delivery complications was collected at follow-up by telephone interviews of 466 (76.5%) women who could be contacted after delivery. A term birth weight was available for 443 babies (72.7%). Multiple logistic regression analysis was used to study the factors associated with macrosomia and low birth weight. Macrosomia was defined as birth weight ≥ 4000g and low birth weight as birth weight <2500 g.

Results: The mean birth weight was 3200 g (SD 450) ranging from 1800 g to 5500 g. Sixteen children (3.6%, 95% CI 2.2-5.8) were born with low birth weight and 26 babies were macrosomic (5.9%, 95% CI 4.0-8.5). Gestational diabetes (GDM) and marital status were independently associated with increased risk of macrosomia whereas, compared to housewives, women who were self-employed had reduced risk of macrosomic delivery. When previous stillbirth and birth weight of the previous child were added to the model (n=282), only GDM (3.43, 95% CI 1.01-11.64) and birth weight of the previous child (OR 2.29 per kg, 95% CI 1.13-4.68) remained significantly associated with macrosomic delivery. Presence of hypertension was the main predictor of low birth weight (OR 3.75, 95% CI 1.11-12.68).

Conclusion: Prevalence of macrosomia was higher than that of low birth weight in infants of women above 19 years in the capital city of Tanzania. Women with GDM or a previous macrosomic child had an increased risk of giving birth to a macrosomic infant. Hypertension was independently associated with low birth weight. Proper management of women with GDM and hypertension during pregnancy is necessary to reduce the risk of adverse birth outcomes.

Introduction

Foetal macrosomia is associated with an increased risk of morbidity and mortality to both the pregnant woman and her new born. It is usually defined as birth weight greater than or equal to 4000-4500 g, or > 90th percentile or two standard deviations of birth weight for gestational age [1]. In the developing countries, prevalence of macrosomia in 23 countries ranged from 0.5% in India to 13.9% in Algeria [2]. Risk factors for macrosomia include maternal age, height, higher parity, infant of male sex, post term pregnancy, diabetes, gestational diabetes mellitus (GDM), and maternal obesity [2, 3].

Likewise, low birth weight defined as weight at birth less than 2500 g regardless of gestational age, is an indicator for maternal and child ill-health and nutritional status [4]. It is associated with an increased mortality rate in the first year of the infant's life, developmental problems in childhood and the risk of various diseases in adulthood [5, 6]. For example, in China and in Nigeria early life exposure to famine was a risk for hyperglycaemia later in life, the association being aggravated by exposure to a Western diet in adulthood [7, 8]. Globally, it is estimated that 20 million infants are born with low birth weight, about 96% of them in the developing countries [4].

Several studies have associated both low birth weight and macrosomia with increased risk of metabolic syndrome later in life. A study in Taiwan reported that children with macrosomia or with low birth weight had 2 to 3 times increased risk for type 2 diabetes when compared to the reference group after adjustment for age, sex, BMI, family history and socioeconomic status [9]. The authors also observed more frequently components of the metabolic syndrome, such as obesity and high blood pressure, among subjects born with high birth weights. Also other studies reported specifically low birth weight [6] or macrosomia [10, 11] as a risk factors for type 2 diabetes, obesity and hypertension in young adults.

Various diseases and health conditions have been associated with birth weight and delivery complications. Studies in Tanzania have shown that anaemia during pregnancy results in low birth weight, still births and increased risk of delivery complications [12, 13]. In contrast to many studies which associate hyperglycaemia with macrosomia, Darling and others [14] reported an increased risk of low birth weight among Tanzanian women with hyperglycaemia during pregnancy. A recent study reported a prevalence of GDM of 8.4% in urban area in Tanzania [15]. The co-

existence of GDM, hypertension, obesity, HIV infection and anaemia may contribute to delivery complications especially when each is poorly managed. We therefore assessed prospectively the risk of adverse birth outcomes, low birth weight and macrosomia among women in Tanzanian urban region.

Methods

Study population

The study was a prospective cohort, part of a larger study conducted in 2011 through 2012 which included selected antenatal care facilities in rural and urban Tanzania. The recruitment involved pregnant women ≥20 years. and at ≥ 20 weeks of gestation during their usual antenatal clinic (ANC) visit [15].

A total of 609 pregnant women attending ANC during the survey period in six selected health facilities in Dar es Salaam, an urban region in the East Coast of Tanzania consented to participate. All women with previously diagnosed type 1 or type 2 diabetes mellitus, those with sickle cell anaemia, already known twin pregnancy and those with non-African origin were excluded. Details are given elsewhere [15]. Women were examined during their usual ANC visit at a mean of 28 gestational weeks and followed up until delivery using mobile telephone communication. The study protocol was approved by Tanzania National Institute of Medical Research and permission to conduct the study was provided by Sokoine University of Agriculture, the District Directors and District Medical Doctors of Ilala, Temeke and Kinondoni districts (Dar es Salaam).

Data collected during recruitment

Socio-demographic information was obtained using a structured pretested questionnaire which was administered through face to face interview. Maternal demographic and clinical information that is routinely captured at the first prenatal visit was extracted from the ANC cards. Information on current pregnancy such as gestational age, gestational age when ANC was started, weight during first visit, HIV status and information related to previous pregnancies, including prior stillbirth, and personal or family history of diabetes mellitus was obtained from ANC maternity card with verification from the mother. Gestational age is usually estimated using the last menstrual period as reported by the mother during the first ANC visit. Age and birth weight of the previous child was obtained from the mother by recall.

Anthropometric measurements were done during antenatal visit at the health facility. Weight of the mothers (in kg) was measured using Seca electronic scale

(Seca Gmbh and Co.kg 22061, Hamburg, German). Height (in cm) was measured without shoes using height measuring board (Shorr productions, Maryland USA). It was categorized into two categories, that is <150 cm and ≥150 cm, based on the Tanzanian antenatal guideline.

Mid-upper-arm circumference (MUAC) was measured using a non-stretching MUAC tape and recorded to the nearest centimeter. Since most of the women appeared late to the clinic (gestational age at booking ranged 8-32 weeks with mean 20 weeks), it was difficult to obtain pre-gestational weight. MUAC is known to be relatively stable during the course of pregnancy and it was highly correlated with pre-pregnancy BMI [16, 17], hence we used MUAC as a proxy for BMI as explained elsewhere [15]. MUAC was further divided into quartiles which were numbered sequentially from Q1 (the group with lowest MUAC values ≤24.5 cm) to Q4 which was the group with highest MUAC values (≥29.0cm).
Blood glucose was measured in capillary blood at fasting state and at two hours after 75 g oral glucose tolerance test using HemoCue Glucose B-201 (Ängelholm AB, Sweden) and recorded in mmol/L. Diagnosis of GDM was based on WHO criteria [18].

Haemoglobin (Hb) concentration were measured in capillary blood using HemoCue Hb 201+ Haemoglobin photometer (HemoCue AB, Ängelholm, Sweden) and recorded to the nearest 0.1 g/dl. Women were classified as anaemic (Hb<11 g/dl) or normal Hb (≥11 g/dl) [19].
Systolic and diastolic blood pressure (BP) was measured from mid-upper-arm of the left side while the respondent was sitting and relaxed for 10 minutes before the actual measurement, using a digital BP device (Microlife BPA100, Widnau, Switzerland). Two readings were taken with an interval of five minutes to ten, and the average systolic and diastolic BP was recorded in mmHg. Hypertension was defined as systolic BP of 140mmHg or higher and/or diastolic BP of 90mmHg or higher. Hypertension disorders of pregnancy (HDP) included chronic hypertension, hypertension with proteinuria and hypertension diagnosed after 20^{th} week of gestation [20].

Women were requested to collect midstream urine on the spot in a provided sterilized disposable plastic container. Urine samples were tested immediately for glucose, ketones, leucocytes and protein using dipstick made with a color sensitive pads (urine strip 10 C, Dialeb GmbH, Austria). Women were considered with

proteinuria when the dipstick was +1 or more in the absence of urinary tract infection [21].

Physical activity was assessed retrospectively by using the short form of the International Physical Activity Questionnaire (IPAQ) which was translated into Kiswahili. Catergories of low, moderate or high physical activity level were calculated using the syntax provided in the IPAQ manual. Dietary diversity data were collected using a dietary diversity questionnaire, as described elsewhere [15]. Total dietary diversity score was divided into three categories and classified as low (0 to 5), medium (6 to 8) and high (9 to 16).

Data collected during follow up

Birth outcome data were collected from mothers using mobile telephone interview. The primary outcome of the study was birth weight. Other outcomes included mode of delivery, preterm births, stillbirths, neonatal death, malformation and reasons for Caesarean section.

During recruitment, participants were informed about the follow-up telephone interview to collect data on birth outcomes. Among the 609 women recruited 530 (87%) provided telephone numbers so that they could be contacted after delivery. Among those who provided their telephone contacts, 64 (12%) could not be reached and we managed to communicate with 466 mothers (76.5%). Data on overall birth outcomes were available for 458 women, whereas birth weight data was available for 443 women (Figure 5.1).

Telephone interviews as a method for data collection is regarded as a useful method due to flexibility and cost effectiveness especially if it is a follow-up [22, 23]. According to TDHS 2010, 78% of Tanzania urban residents own mobile telephones [24] and a survey conducted in 2010 in Dar es Salaam, mobile telephone ownership was more than 80% [25]. In our study, 87% of the participants provided telephone contacts and overall 77% could be contacted.

Infants birth weight was categorised as low birth weight (<2500 g), normal birth weight (2500 to 3999 g) and macrosomia (≥4000 g) when born between 37 and 42 gestational weeks [26]. Preterm birth was defined as live birth before 37 gestational weeks. Stillbirth was defined as baby who was born without any sign of life after 24 gestational weeks. Neonatal death included children who died within a period of 28 days after birth.

Data analysis

Data were entered and analysed using IBM SPSS program version 19.0, Chicago, IL. Results were recorded as means and standard deviations for continuous variables and numbers and percentages for the categorical variables. Students T-test for continuous variables and Chi-Square test for categorical variables were used to assess differences in characteristics according to follow-up status. Comparison of birth outcomes in women with and without GDM and those with and without HDP were done using Chi-square test. Differences in continuous and categorical variables according low birth weight and macrosomia compared to those with normal birth weights were assessed by ANOVA or Chi-square test, respectively.

Logistic regression analysis was done to determine the main factors associated with macrosomia and low birth weight. In multiple logistic regression models, confounders with $p< 0.2$ in bivariate analyses were included to examine the adjusted association of these factors with the delivery of a macrosomic or low birth weight baby. For logistic regression, birth weight was dichotomized to normal and high when macrosomia was the outcome and as low and normal when low birth weight was the outcome. In both the low birth weight and macrosomia models, the first model included all women with birth weight data, while the second model included previous stillbirth and previous birth weight as covariates, hence primiparous (n=161) were excluded.

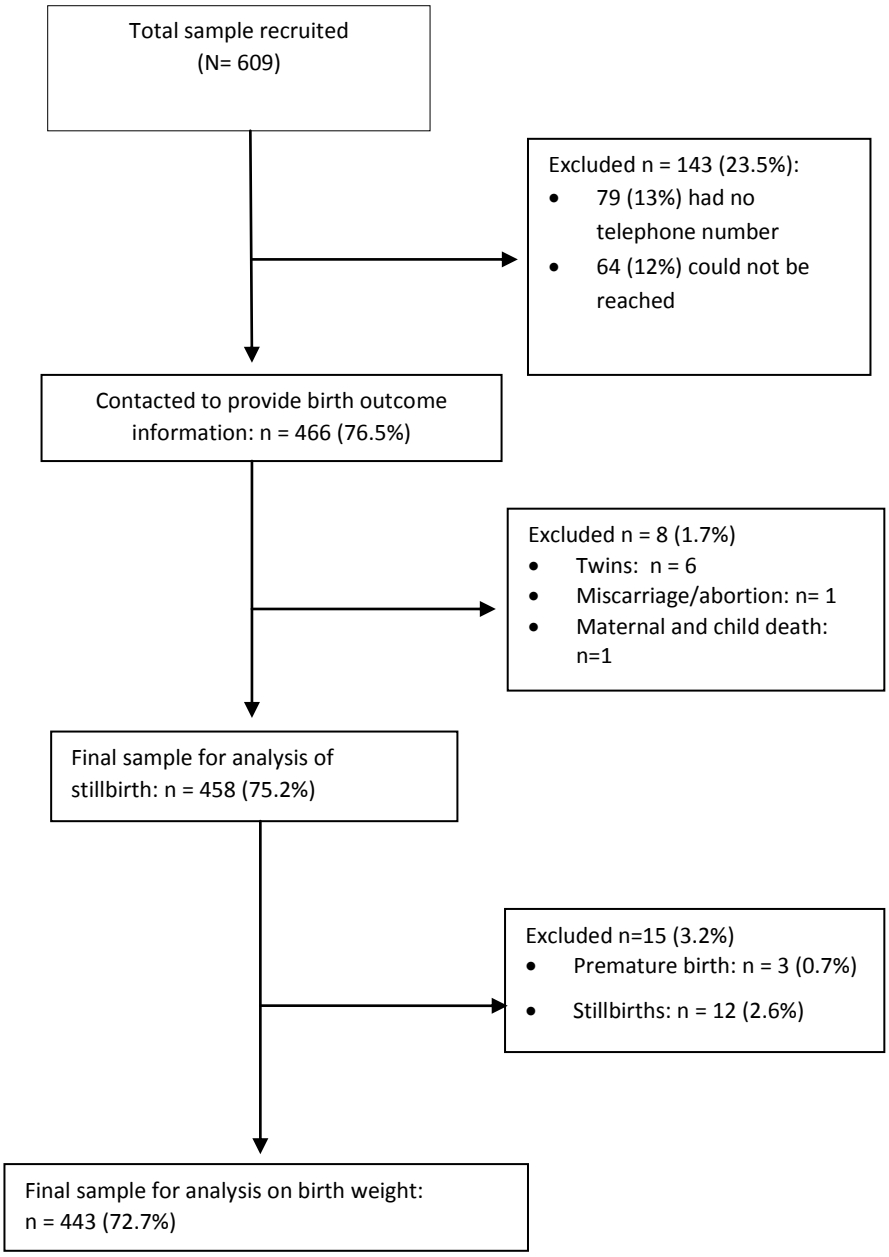

Figure 5.1: Flow diagram of the cohort

Results

Sample characteristics of the missed and accessed study population

Women with complete data were on average older (27.8 vs 26.4 yrs.), taller (155.6 vs 154.5 cm) and had higher MUAC (27.5 vs 26.5 cm) compared to women who were lost to follow-up (Table 5.1). Other anthropometric, socio-demographic and biochemical indices were similar between the two groups.

Table 5.1: Anthropometric, Sociodemographic and biochemical indices: Comparison between loss to follow-up and the available study group of pregnant women during the survey in Dar es Salaam 2011/2012

	Missing (n = 143)		Available (n = 466)		
Variable	**Mean**	**SD**	**Mean**	**SD**	**P-value**
Age (years)	26.4	4.8	27.8	5.1	0.002
Height (cm)	154.5	5.8	155.6	6.0	0.05
MUAC (cm)	26.5	3.4	27.5	3.8	0.005
BMI at booking (kg/m^2)	24.5	4.0	25.3	4.6	0.054
Gestational age at booking (wks.)	18.4	4.1	17.8	4.7	0.165
Gestational age during survey (wks.)	27.5	5.0	28.3	4.7	0.085
Parity	2.4	1.2	2.4	1.3	0.576
Systolic BP (mmHg)	115.0	14.0	114.7	15.5	0.865
Diastolic BP (mmHg)	72.1	10.8	72.6	11.8	0.679
Haemoglobin (g/dl)	10.0	1.6	10.1	1.6	0.480
Fasting BG (mmol/L)	4.5	0.8	4.6	1.0	0.215
2-hr BG (mmol/L)	6.0	1.1	6.1	1.1	0.577
	n	**%**	**n**	**%**	
Education:					
Informal	10	7.0	28	6.0	0.252
Primary	105	73.4	315	67.6	
Secondary or higher	28	19.6	123	26.4	

Marital status					
Married	115	80.4	392	84.1	0.300
Single	28	19.6	74	15.9	
Primary source of income					
Housewife	78	54.5	212	45.5	0.102
Salary/wage	23	16.1	73	15.7	
Self employed	42	29.4	181	38.8	
HIV status					
Negative	128	89.5	422	90.6	0.711
Positive	15	10.5	44	9.4	
Family history of Type 2 diabetes					
No	125	87.4	396	85.0	0.469
Yes	18	12.6	70	15.0	
Parity					
Prime	38	23.6	133	28.5	0.647
Multipara	105	73.4	333	71.5	

Association of GDM and HDP with birth outcome

We analysed information collected on birth outcome from 466 women who were recruited in our study as shown in Figure 5.1. Caesarean delivery was reported by 6.3% and the reasons were either preeclampsia (n=4), previous scar (n=7), obstructed labour (n=5), macrosomia (n=3), pelvic disproportional (n=2), breach (n=6) and placenta previa (n=2). Two out of the three preterm births were associated with hypertension. There was no clear association between GDM and birth outcomes. Comparing delivery complications among women with and without HDP, 7.5% versus 2.2% had stillbirths, 5% versus 1.7% reported neonatal deaths, while 5% versus 0.2% experienced preterm delivery respectively (Table 5.2).

Table 5.2: Association between GDM and HDP with selected birth outcome variables

Variable	Normal (N=413) n (%)	GDM (N=45) n (%)	p-value	Normal (N=418) n (%)	HDP (N=40) N (%)	p-value	Total n (%)
Normal	390 (94.4)	42 (93.3)		399 (95.5)	33 (82.5)		432 (94.3)
Stillbirths	12 (2.9)	0 (0.0)		9 (2.2)	3 (7.5)		12 (2.6)
Neonatal deaths	7 (1.7)	2 (4.4)	0.291	7 (1.7)	2 (5.0)	0.001	9 (2.0)
Malformations	2 (0.5)	0 (0.0)		2 (100)	0 (0.0)		2 (0.4)
Preterm delivery	2 (0.5)	1 (2.2)		1 (0.2)	2 (5.0)		3 (0.7)
Mode of delivery							
Normal	389 (94.2)	40 (88.9)	0.116	392 (91.4)	37 (8.6)	0.751	429 (93.7)
Caesarean	24 (5.2)	5 (11.1)		26 (6.2)	3 (10.3)		29 (6.3)

GDM: Gestational diabetes mellitus
HDP: Hypertensive disorders during pregnancy

Factors associated with low birth weight and macrosomia

Birth weight ranged from 1800 g to 5500 g with a mean of 3200 g (SD 450). Sixteen infants (3.6%; 95% CI 2.2-5.8) had low birth weight while 26 were macrosomic (5.9%; 95% CI 4.0-8.5). Mean birth weight for the macrosomic infants was 4260 g (SD 364) while for the low birth weight it was 2194 g (SD 181).

Fifty-one percent of the children were female. The prevalence of macrosomia was almost twice as high in boys (7.8%) compared to girls (4.0%). Among the 45 women who were diagnosed with GDM the frequency of macrosomic infants was higher (18.2%) than in normoglycaemic women (4.5%) (Table 5.3). None of the GDM women had a child with low birth weight. Among women with HDP the prevalence of low birth weight was significantly higher (11.4%) compared to the normotensive group (2.9%). In univariate analysis, besides GDM and hypertension, a significant difference in birth weight was observed among maternal occupation categories. Housewives had more frequent macrosomic infants while self-employed women had more frequently low birth weight. In addition, married women had more frequent a low birth weight infant while single women had more frequent a macrosomic child. Although not statistically significant, a higher occurrence of macrosomia was observed in women with previous macrosomic child (13.2% vs 5.7%), multiparity (6.7% vs 3.9%) and those with family history of diabetes (9.0% vs 5.3%).

Table 5.3: Prevalence of low birth weight and macrosomia according to different maternal characteristics among women attending ANC in Dar es Salaam city (2011/2012)

Characteristics of the mother	LBW (n=16)		Normal (n=401)		Macrosomia (n=26)		
	Mean	SD	Mean	SD	Mean	SD	P value
Birth weight current child (g)	2194	180	3212	323	4265	364	0.000
Birth weight previous child (g)	3121	520	3307	684	3668	488	0.040
Gestational age at recruitment (weeks)	26.9	5.2	28.4	4.7	28.6	5.1	0.477
Gestational age at starting ANC (weeks)	16.9	5.1	17.9	4.7	18.3	4.5	0.653
	N	%	n	%	n	%	P value
Sex of the child							
Male	7	3.2	193	88.9	17	7.8	
Female	9	4.0	208	92.0	9	4.0	0.213
Marital status							
Married	15	4.1	337	91.1	18	4.9	
Single	1	1.4	64	87.7	8	11.0	0.076
Occupation							
Housewife	5	2.5	176	88.4	18	9.0	
Salary/wage	1	1.4	67	95.7	2	2.9	0.035
Self employed	10	5.7	158	90.8	6	3.4	
Education							
Informal	1	3.4	24	92.3	1	3.4	
Primary	13	4.3	274	90.4	16	5.3	0.619
Secondary or higher	2	1.8	103	90.4	9	7.9	

Age							
<25 yrs.	2	1.5	123	91.8	9	6.7	0.265
≥25 yrs	14	4.5	278	90.0	17	5.5	
Height							
<150 cm	3	4.7	58	90.6	3	4.7	0.812
≥150 cm	13	3.4	348	9.05	23	6.1	
MUAC quartiles							
Q 1 (<24.5 cm)	3	2.9	94	92.2	5	4.9	0.446
Q 2 (24.5 – 26.9 cm)	3	2.7	100	90.1	8	7.2	
Q 3 (27.0 – 29.0 cm)	3	2.8	101	94.4	3	2.8	
Q 4 (>29 cm)	7	5.7	106	86.2	10	8.1	
GDM							
Yes	0	0.0	36	81.8	8	18.2	0.001
No	16	4.0	365	91.5	18	4.5	
Hypertension							
No	12	2.9	371	90.9	25	6.1	0.027
Yes	4	11.4	30	85.7	1	2.9	
Anaemia							
Yes	10	3.3	276	90.5	19	6.2	0.772
No	6	4.3	125	90.6	7	5.1	
HIV status							
Positive	1	23.0	39	90.7	3	7.0	0.853
Negative	15	3.8	362	90.5	23	5.8	

Parity							
Prime	2	1.6	121	94.5	5	3.9	0.166
Multipara	14	4.4	280	88.9	21	6.7	
Family history of diabetes							
Yes	0	0.0	61	91.0	6	9.0	0.127
No	16	4.3	340	90.4	20	5.3	
Physical activities							
Low	4	4.2	84	87.5	8	8.3	0.422
Medium	9	3.9	213	92.2	9	3.9	
High	3	2.6	104	89.7	9	7.8	
DDS							
Low (<	4	4.3	83	88.3	7	7.4	0.382
Medium	12	4.1	265	91.1	14	4.8	
High	0	0.0	53	91.4	5	8.6	
Previous stillbirth							
No	9	3.8	211	90.6	13	5.6	0.021
Yes	5	10.4	37	77.1	6	12.5	

LBW: low birth weight; GDM: gestational diabetes mellitus; DDS: Dietary diversity score; MUAC: mid upper arm circumference

Two models were fitted to assess the association of risk factors with macrosomia. The first model included GDM, child's sex, marital status and occupation. Women with GDM had about five times higher risk of giving birth to a macrosomic infant compared to normoglycemic ones (OR 4.77, 95% CI 1.87-12.21) and single women had three times increased risk of a macrosomic child (OR 3.23, 95% CI 1.27-8.22) compared to married women. Furthermore, compared to housewives, women who were self-employed had a reduced risk of macrosomic delivery (OR 0.36, 95% CI 0.16-0.95). Variables included in the second model were GDM, marital status, occupation, child's sex, birth weight of the previous and still birth child, and only

GDM (3.43, 95% CI 1.01-11.64) and birth weight of the previous child (OR 2.29, 95% CI 1.13 – 4.68) remained significantly associated with macrosomic delivery (Table 5.4).

Table 5.4: Crude and adjusted associations between selected risk factors and macrosomic births among women attending ANC in Dar es Salaam city (2011/2012)

Variable	Crude OR	95% CI	P value	Adjusted OR^	95% CI	P-value
Model 1 (n=443)						
GDM	4.70	1.91 - 11.57	0.000	4.77	1.87 – 12.21	0.001
Childs sex (Male)	2.05	0.89 – 4.70	0.09	1.93	0.82 – 4.54	0.134
Marital status (Single)	2.41	1.00 – 5.77	0.043	3.23	1.27 – 8.22	0.014
Occupation						
Housewife	1			1		
Formal employment	0.29	0.07 – 1.31	0.108	0.23	0.05 – 1.09	0.062
Self employed	0.34	0.14 – 0.93	0.034	0.36	0.16– 0.95	0.038
Model 2 (n=282)*						
GDM	4.58	1.49 – 14.09	0.008	3.43	1.01 – 11.64	0.048
Marital status (Single)	2.25	0.76 – 6.63	0.141	2.32	0.72 – 7.51	0.160
Occupation						
Housewife	1			1		
Formal employment	0.53	0.11 – 2.48	0.418	0.46	0.09 – 2.32	0.343
Self employed	0.39	0.14 – 1.16	0.091	0.43	0.14 – 1.32	0.139
Birth weight of previous child (kg)	2.16	1.12 – 4.16	0.021	2.29	1.13– 4.68	0.022
Previous stillbirth	2.43	0.87 – 6.75	0.008	2.65	0.86 – 8.20	0.090

*Including only multiparous women

Similarly, two models were fitted to assess factors associated with low birth weight (Table 5.5). Variables included in the first model were HDP and occupation, and the second model included HDP, occupation and previous still birth. In both models,

women with HDP had about four times increased risk for low birth weight (OR: 4.10, 95% CI 1.23-13.66 and 3.75, 95% CI 1.06 -13.25, for the first and second model, respectively) compared to those who had normal blood pressure.

Table 5.5: Crude and adjusted associations between selected risk factors and macrosomic births among women attending ANC in Dar es Salaam city (2011/2012)

Variable	Crude OR	95% CI	P value	Adjusted OR*	95% CI	P-value
Model 1 (n=443)						
HDP	4.26	1.29 – 13.98	0.017	4.10	1.23 – 13.66	0.021
Occupation						
House wife	1			1		
Formal employment	0.56	0.07 – 4.89	0.602	0.62	0.07 – 5.48	0.670
Self-employment	2.37	0.79 – 7.06	0.123	2.39	0.79 – 7.21	0.120
Model 2 (n=282)*						
HDP	4.07	1.18 – 13.96	0.026	3.75	1.11– 12.68	0.033
Occupation						
House wife	1			1		
Formal employment	0.83	0.09 – 7.63	0.866	0.98	0.10 – 9.38	0.993
Self-employment	2.37	0.71 – 7.91	0.161	2.44	0.71 – 8.34	0.154
Previous stillbirth	2.91	0.93 – 9.10	0.067	2.67	0.83 – 8.62	0.101

*Included multiparous

Discussion

In our cohort, stillbirths occurred more often among women with hypertension compared to normotensive ones, but GDM was not significantly associated with adverse birth outcomes. Regarding birth weight, 5.9% of the infants were

macrosomic and 3.6% had low birth weight. GDM, occupation, marital status and previous macrosomia were independent risk factors for macrosomia, while hypertension was the main risk factor for low birth weight.
GDM is a known risk factor for other delivery complications. However, we did not find a significant association between GDM and stillbirths, preterm delivery, malformations or neonatal deaths, although the number of adverse birth outcomes, especially Caesarean deliveries, was higher among GDM. Due to few cases the power to detect such associations may have been limited. Furthermore, measurements of blood glucose and blood pressure were done at baseline, at mean gestational age of 28 weeks, and women were informed of their status, and hence some lifestyle modification may have taken place which might have improved birth outcomes to some extent.

We found significant associations of HDP with stillbirth and low birth weight. Other studies suggest that high blood pressure is associated with placental dysfunction which can result in foetal growth restriction [27]. Similar results were reported by other studies in Africa [28-30] and in a population-based case-control study in India [31].

The occurrence of low birth weight in our study was lower than in earlier studies in urban Tanzania [32, 33], and was about half of the national estimates (TDHS 2010). This may be due to the high maternal age of our study population since we excluded teenagers [34]. A recent study in Dar es Salaam reported a high prevalence of low birth weight among underweight women and also noted an increase in pregnancies in older age in recent years [35].In our study the prevalence of underweight among pregnant women was low; using a MUAC cut-off of 22 cm, underweight was prevalent in 3.2% while using BMI at booking (<18.5 kg/m^2) underweight was 3.4%. Conversely, the prevalence of obesity (MUAC ≥33 cm) was 9.9% and using BMI at booking of ≥30 kg/m^2 it was 14.7%. The current trend of women becoming pregnant at more advanced age, the increased prevalence of obesity and overweight in women of reproductive age and the existence of diabetes during pregnancy are likely to contribute to the observed number of macrosomic infants.

A review by Barro et al [36] reported that about 50% of the low birth weights in low and middle income countries are preterm. In our study we excluded two preterm births, the rest of the women reported to have delivered at full term, which may explain the low occurrence of low birth weight in our study population. It is also

possible that some children who were stillborn had low birth weight, but their weight was not accessed.

The observed prevalence of macrosomia was within the range reported in other African studies [37-39]. It is important to note that variation in incidence of macrosomia may be due to different weight cut-offs used in different studies. Compared to our study a higher incidence of 8.1% and 14.6% was reported in two Nigerian studies [37, 38] with a similar classification for macrosomia. Using a higher cut-off (≥4500 g), a lower frequency was reported in another Nigerian study [40].

Women with GDM and those with previous macrosomic child had an increased risk of macrosomic deliveries even after adjustment for MUAC and child's sex. GDM is one of the commonly known predictor of macrosomia [2, 39]. The elevated glucose level in the foetus as a result of maternal hyperglycaemia may result in overstimulation of the foetal pancreas and foetal hyperinsulinemia, and hence foetal growth [41].

BMI is a known risk factor for macrosomia [42], and has been shown to be a stronger predictor compared to maternal glucose levels [43]. In our study, GDM and birth weight of the previous child were predictors of macrosomia, but we did not find a significant association between maternal MUAC quartiles with macrosomia. It is possible that high pregnancy weight gain or high waist circumference before conception could be a determinant of macrosomia in our study population. Pre-pregnant waist circumference was, for example a risk factor for macrosomia independent of BMI among black women [44]. However, pre-pregnancy waist and weight gain during pregnancy were not assessed in our study.

Single women were more likely to give birth to a macrosomic infant compared to married ones. This is contrary to an earlier study in Tanzania where single mothers were more likely to give birth to low birth weight infants [32]. The differences could be due to characteristics of the studied population; this previous study had a mixture of urban and rural women while our study was done in the urban area. Self-employed women and those with formal employment were less likely to have a macrosomic infant compared to housewives, which could be due to a more active lifestyle among these two groups.

Studies in Tanzania and in Ethiopia showed that women with HIV infection were at an increased risk of delivering a low birth weight infant [35, 45, 46]. Although we observed a high prevalence of HIV (9.7%), it was not associated with still birth or

low birth weight. About two thirds of the HIV positive women (62.8%) were taking micronutrient supplements which might have improved birth outcome [47].

Short stature [48] and anaemia [12, 13] are also recognized risk factors for low birth weight. Nevertheless, we did not find a clear association in our study, possibly due to small number of low birth weight deliveries. Other studies identified smoking and alcohol intake as risk factors for low birth weight [49, 50], but in our study only 0.9% of the participants were smoking and about 14% were drinking alcohol and none were associated with low birth weight.

The recall method for assessing birth weight and other delivery outcomes has been used previously in the demographic and health surveys in Tanzania [24]. In the developed countries recall of pre-and perinatal factors was found to be good and in agreement with hospital records [51, 52]. In African studies, maternal recall of child's birth weight was moderately in agreement with recorded values in Uganda for children above four years [53], while it was found to be good in rural Kenya [54]. The accuracy of the recall depended on factors such as maternal education, place of delivery and the time lapse from delivery [53]. In our study there could be bias regarding the birth weight of the previous child, due to the time lapse from previous delivery to current pregnancy. However, for the current child we expect minimal recall bias because of the short time lapse between delivery and the interview and due to prior notification of the participants regarding the follow up. In fact, birth weight was rather being read as recorded on the card immediately after delivery.

Women lost to follow up (23.5%) were on average younger, shorter and had lower MUAC, which are all determinants of birth weight. This limited the variation in age, height and MUAC to some extent, and this could be an additional reason for not finding and association with birth weight in our study. Birth weights might have been slightly over-or underestimated due to inaccurate estimation of gestational age, hence some of the low birth weight might be preterm deliveries, and some macrosomic births might be post term deliveries. Other causes of still births like syphilis and malaria were not addressed [55], but unless the participant was re-infected, the two infections were universally checked and treated. Also, universal malaria prophylaxis for all pregnant women is usually given during ANC visit in the second and third trimester. Finally, the study was conducted in an urban setting (Dar es Salaam) with higher proportions of institutional deliveries compared to

other areas in Tanzania, hence the results cannot be generalized to other parts of the country.

In conclusion, the prevalence of macrosomia was higher than that of low birth weight in offspring of women ≥20 years in Dar es Salaam. Thus, it seems that the double burden of malnutrition exists in the study area even at the infancy stage, where low birth weight and macrosomia exist in the same population. Women with GDM diagnosed during usual ANC visits had an increased risk for macrosomia. Hypertension during pregnancy was associated with low birth weight regardless of maternal age and MUAC, and it was a risk factor for stillbirth. This highlights the importance of screening and lifestyle interventions for women at risk.

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Chapter 6

Including blood glucose testing during antenatal clinic visits in Tanzania: Opportunities and challenges

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(*Under preparation for submission*)

Abstract

Aim: To assess opportunities and challenges for including blood glucose testing during usual antenatal care (ANC) in Tanzania.

Methods: A review of published literature and government documents on maternal and child health care delivery in Tanzania was performed. Additional data were collected through a survey that included 24 randomly selected health facilities (HFs) from Dar es Salaam region. Health workers responsible for ANC from each of the selected HF were interviewed using a pretested structured questionnaire focusing on the practice of screening for gestational diabetes (GDM) during ANC.

Results: The quality of ANC was generally regarded as inadequate due to limited human resources, low level of counselling skills, and shortage of equipment and drugs. The following services were offered by all the surveyed HFs: measurement of blood pressure, weight and height, immunization, education and counselling for HIV and prevention of mother to child transmission, and for pregnancy danger signs. About 92% of the HFs tested urine for albumin and glucose. Out of 12 private HFs surveyed, three (25%) reported to always perform a random blood glucose measurement to all women attending ANC. The cost of this measurement ranged from one to four dollar per sample (1500 to 6000 TZS). According to the ANC health workers, blood glucose testing is important but the government should provide guidelines, materials and training.

Conclusion: Diabetes screening during pregnancy is already in place in most of the ANC in Dar es Salaam by testing urinary glucose and albumin in every woman attending ANC. As the sensitivity of glycosuria for GDM is low, selective blood glucose testing during ANC visits using the existing HIV testing and counselling program as an entry-point may be an option. Studies on the actual cost for such a program including management of GDM in the Tanzanian setting are necessary.

Background

Sub Saharan Africa (SSA) has the highest maternal mortality in the world, with the majority of maternal deaths being attributed to haemorrhage, infections, obstructed labour and hypertension [1, 2]. In Tanzania, there is a slight decrease in maternal mortality from 578 to 454 per 100,000 in the last 10 years, but Tanzania is still among the countries with the highest maternal mortality in SSA [3]. In addition, it is one of the top ten countries with highest stillbirths rate, reported to be >25 per 1000 births [4]. In most cases, interventions to address maternal mortality and stillbirths are implemented in the reproductive and child health (RCH) care during prenatal and postnatal visits. Reproductive and child health clinics, therefore, are considered as a point of care where interventions for prevention, screening and management of GDM could be implemented, starting during antenatal care (ANC).
Although GDM and unrecognized type 2 diabetes mellitus may lead to maternal and foetal morbidity and mortality in SSA, timely diagnosis and management strategies rarely exist in this part of the continent. Studies show that prevalence of GDM in Tanzania has increased from 0% to 5.9% in about 20 years [5, 6]. These findings suggest that something has to be done at the ANC level. The only screening strategy currently in place is urine analysis. A glucose test in urine has low sensitivity in detecting women with GDM, and is therefore not recommended [7, 8]. The International Diabetes Federation recognizes identification and treatment of GDM as a global priority [9]. Every pregnant woman is supposed to attend antenatal clinic (ANC) more than once during the course of the pregnancy, which offers a unique opportunity for education and intervention to prevent adverse pregnancy outcomes and to establish lifestyle changes.

The main objective of this study was to assess existing opportunities and possible challenges for including GDM screening during usual ANC visits in Tanzania. We therefore reviewed literature on the ANC services. Additionally, we conducted a survey among health facilities in an urban setting (Dar es Salaam) to investigate the possibilities of integrating blood glucose testing in the usual ANC regimen within the current protocol. We also investigated the attitude of health care providers regarding screening, counselling and management of GDM. The study was intended to provide information to guide in development of strategies for implementing diabetes screening during pregnancy.

Methods

Review of health care services in Tanzania

Various published reports and scientific studies conducted in Tanzania were reviewed to establish the state of health care services, the main focus being on ANC with reference to the WHO's guides on antenatal care procedures. The internet was searched to identify relevant reports and scientific papers. The literature presented includes the Tanzanian health care system and the Tanzanian ANC system.

Health facility survey

Sampling procedure

A health facility survey was conducted in Dar es Salaam, Tanzania, from February through March 2013. Dar es Salaam region is the largest city in the country with a population of about 4.3 million. According 2010 data the region has 449 HFs, 28 hospitals, 29 health centres and 392 dispensaries. About half of the HFs (244) offer ANC services, 133 being private and 91 being government managed [10].

Health facilities in the region offering RCH services were stratified into hospitals, health centres and dispensaries. All health facilities owned either by individuals, groups of people, faith based organization or parastatal were grouped under private managed HFs. While hospitals were purposively selected, health centres and dispensaries were randomly selected. The number and distribution of the included health facilities is shown in Table 6.1.

Table 6.1: Distribution of health facilities with RCH services according to district

	Hospital		Health centre		Dispensary		Total		
District	**Government**	**Private**	**Government**	**Private**	**Government**	**Private**	**Government**	**Private**	**Total**
Ilala	2	7	2	8	20	16	24	31	55
Temeke	2	2	1	3	26	42	29	47	76
Kinondoni	1	13	2	12	35	30	38	55	93
Total	5	22	5	23	81	88	91	133	224
Sample	3	3	3	3	6	6	12	12	24

Source: RCH report (Regional RCH coordinator)

Data collection and analysis

Pretested structured questionnaire was administered through face to face interview with the in-charge of the ANC services in each health facility. The questionnaire covered quantitative and qualitative information including health facility information, availability of delivery services, availability of health education/counselling, physical assessments, laboratory services, blood glucose testing, costs per sample, equipment and availability of drugs. Other aspects in the questionnaire were personnel training and infrastructure. Respondents were also asked about their views regarding glucose testing for pregnant women attending ANC. A checklist was used to assess ANC facility infrastructure, supplies and equipment and health care practices during ANC clinic. Descriptive analysis was done using IBM SPSS program version 19.0, Chicago, IL. and results were presented as frequencies (number and percentages).The study was approved by the Tanzania National Institute of Medical Research. For the government facilities, permission was also obtained from the district medical officer and the in-charge of the selected health facility. The facility director provided permission for private health facilities.

Results

Literature review

Health service delivery in Tanzania

The health care delivery system in Tanzania is well organized. As per the assessment carried out in 2012, there were a total of 6663 health facilities in the country, comprising 241 (4%) hospitals, 742 (11%) health centres and 5680 (85%) dispensaries [11].

The health care system operates in a model of a pyramid shape, the lowest level (base) being the community HFs owned by the village government. The second level includes the dispensaries and is the primary level for RCH services (Figure 6.1). The next level consists of health centres which also receive referrals from dispensaries. Higher up in the pyramid are the district hospitals, which also serves as district hospitals; together with the dispensaries and health centres they constitute the primary health care [12]. The regional hospitals receive referrals from the district hospitals or from the health centres depending on the severity of the problem. Most government and private dispensaries and health centres offer

ANC services daily, and women with pregnancy danger signs are referred either to the health centre, to the district referral hospital or regional referral hospital.

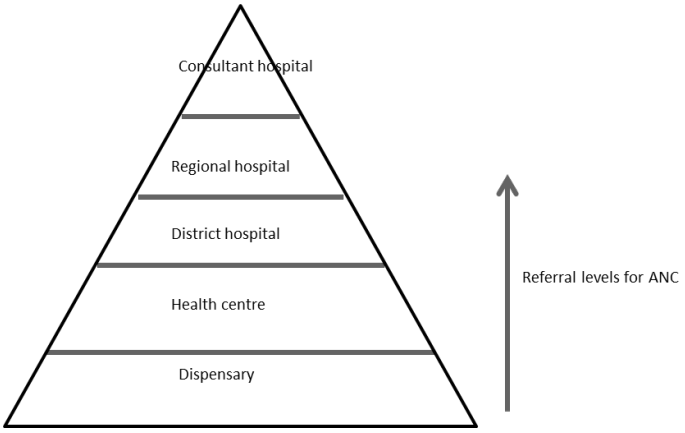

Figure 6.1: Organization of health care system in Tanzania (Adopted from the Ministry of Health website: http://www.moh.go.tz/index.php/health-services-in-tanzania)[13]

Limited budget has always been a problem in the Tanzanian health care system. For example, in 2010/2011 the health budget was 9.8% of the national budget compared to 15% recommended by Abuja Declaration [14]. The government contribution to health was 54% and some interventions for prevention and counselling for HIV/AIDS and malaria depended mainly on foreign funds [15]. With regard to human resources, on average, only one third of the posts are filled, of which dispensaries and health centres have a shortage of more than 66% [14]. A study in five districts in the Southern part of Tanzania showed that only 14% of the recommended number of nurses and 20% of the clinical staff has been employed at the facility [16].

In 2003, the Tanzania Diabetes Association in collaboration with the Ministry of Health and Social Welfare established diabetes clinics which are currently run by the district, regional or national referral hospitals [17]. In 2006, there were 29 diabetes clinics, the majority being within the regional hospitals. These clinics offer free consultations and the government subsidises medical and laboratory costs [18]. During ANC visits, women who are detected with hyperglycaemia from urine analysis or who show typical symptoms of diabetes during pregnancy are referred to the diabetes clinic.

Antenatal care in Tanzania

Antenatal care is important for a wide range of preventive and curative services and it is offered in RCH. This is also where pregnant women are informed on the importance of being attended by skilled health personnel for delivery and post-delivery care.

In Tanzania, maternal and child health services started in 1974. Since then, several guidelines and strategies for promoting improved maternal and child health have been developed and disseminated [19, 20]. This included the reproductive and child health strategic plan, with the main goal to reduce maternal, neonatal and child morbidity and mortality by strengthening health systems and increasing access to RCH services[19, 21].According to the National Health Policy, all antenatal services are free; in addition pregnant women are exempted from paying health service user fees at the government health facilities. However, this is not implemented fully, and for some services such as laboratory services and drugs pregnant women are forced to pay. This is often the case when a particular service is not offered and when drugs are out of stock at the health facility [16]. In private facilities offering RCH services, women pay for almost every service, except family planning, HIV and counselling on prevention of mother to child transmission (PMTCT) that are supported by the government.

In 2001 the World Health Organization (WHO) issued guidance on a new model of ANC called goal-oriented or focused antenatal care (FANC), for implementation in developing countries [22, 23]. Tanzania has adopted this WHO recommendation of a minimum of four ANC visits during pregnancy, since 2002. The FANC guideline recommends that during these four visits, blood pressure, haemoglobin estimation, weight gain, testing of urine for albumin and glucose, fundal height, foetal lie and movements or heart rate are assessed. Measurement of height and testing for syphilis, HIV status, blood group and Rhesus factor are recommended to be done at least once during the course of pregnancy. Other ANC services include preventive strategies for tetanus, malaria, anaemia and mother to child HIV-transmission, education on possible complications and preparation for delivery care of new-born, family planning as well as treatment of detected ill-health [22].

Currently, PMTCT services have been integrated within the maternal, neonatal and child health platform, where HIV and syphilis testing is mandatory to all pregnant women attending ANC [24]. It is recommended that those who were not tested during pregnancy, they should be checked during labour or postnatal care.

There is high coverage of HIV testing and counselling. In 2011/2012, about 80% of pregnant women tested for HIV and 76% received results [25]. The incidence of testing and receiving results was higher in urban areas (89.6%) compared to rural areas (73.2%), with also a higher proportion of women receiving results in the urban (89.6%) compared to rural areas (73.2%).

Quality of Antenatal Care

Several studies have attempted to assess the quality antenatal and childbirth care in Tanzania. Most of the studies were conducted in the rural areas. Duysburg et al (2013) assessed the quality of antenatal and child care in selected rural health facilities in Burkina Faso, Ghana and Tanzania [26, 27]. They reported satisfactory quality of ANC and child birth services, but noted that there was poor and less efficient counselling as only one out of three women was counselled on pregnant danger signs. Moreover, there was poor health education, laboratory examinations were rarely performed, and there was inadequate monitoring of the mother and the newborn during childbirth. Poor counselling was also reported by Pembe et al. [28].

A cross-sectional study in Tanzania, Uganda and Burkina Faso assessed the health worker's compliance to the FANC [29]. The authors revealed that there was substantial variation in the provision of antenatal care services among health facilities within and among the country sites, but generally, the workers omitted some of the practices stipulated in the FANC guidelines. Also, reagents for laboratory tests and drugs as outlined in the guidelines were often out of stock in most facilities. Similar findings of failure to follow FANC guideline were reported by different studies done in Kilombero, Ngorongoro and Rufiji districts of in Tanzaniaand shortage of materials and high workload due to absentism were mentioned as reasons for not following the guideline [30-32].

In a rural clinic in Morogoro region, Nyamtema et al [33] observed that attendance was generally good since 83% of the mothers had at least two visits. Necessary equipment for measuring blood pressure, stethoscopes, weighing scales, HIV test kits, and malaria prevention drugs, mebendazole and folic acid were available in more than 90% of the HFs. However, glucose and albumin sticks were rarely available. They further concluded that there was a substandard quality of care resulting from shortage of staff and lack of material resources [33]. Other researchers assessed the reasons for late initiation of ANC in selected rural districts

and revealed perceived poor quality of care, including poor patient–provider relationship, late recognition of pregnancy and lack of social and economic support from the partner as the most common reasons for starting ANC late [34, 35].

Gupta et al [36]assessed factors associated with attending four or more ANC visits. They observed that being informed about signs of pregnancy related complications, having blood pressure measured and having urine and blood samples taken during the ANC visit, were associated with higher rates of ANC visits. This study concluded that efficiency in ANC depended on the number of staff, structural quality of care, process quality of care and perceived quality of care.

In conclusion, general attendance to ANC in Tanzania is good. However, the quality of care varies across the country. Observed substandard ANC services were mainly attributed to inadequate human workforce (number and skills) and lack of regular supply of materials and drugs as well as limited socioeconomic support leading to less number of visits or late initiation of ANC.

Results from the survey

Among the 24 HFs in Dar es Salaam investigated, the average number of women attending ANC per day was 28 (range 10-75). Average gestational age for starting ANC was 20 weeks. Blood pressure, height and weight measurements were taken in all HFs. Additionally, immunization, education and counselling for HIV, PMCTC, and pregnancy danger signs were also offered in all surveyed HFs. However, emergency transport was available in less than half of the HFs. Five HFs did not have delivery services and one faith based centre did not have family planning education due to religious reasons (Table 6.2).

Table 6.3 shows the laboratory assessments that are performed at the HF and whether the women had to pay or not for the service. All biochemical assessments were done in the general laboratory except for syphilis and HIV tests which were done by RCH nurses at the ANC clinic. In few of the clinics, biochemical assessments were free of charge. Urine test for glucose and albumin was a common practice in almost all clinics (91.7%).

Table 6.2: ANC services, counselling and availability of facilities and equipment in the surveyed health facilities

Service	N	%
Immunization	24	100
Family planning	23	95.8
HIV/AIDS	24	100
PMTCT	24	100
HemoCue (Hb)	21	87.5
Emergency transport	10	41.7
Computer	17	70.8
Internet connection	8	33.0
Waiting room	20	83.3
Glucometer	12	50.0
Health education and counselling		
Diet and nutrition	21	87.5
Danger signs	24	100
Hygiene	23	95.8
Breast feeding	22	91.7
STI	24	100
Medicine use	24	100

Hb: Haemoglobin; PMTCT: Prevention of mother to child transmission; STI: Sexual transmitted infections

Table 6.3: Laboratory tests and charges

Test	Is the test done						Charged			
	Always		Rarely		Never		Yes		No	
	n	%	n	%	n	%	n	%	n	%
Malaria (BS)	20	83.3	4	16.7	0	0.0	16	66.7	8	33.3
Hb	20	83.3	4	16.7	0	0.0	14	58.3	10	41.7
Blood group	15	62.5	8	33.3	1	4.2	14	60.9	9	39.1
HIV	23	95.8	1	4.2	0	0.0	3	12.5	21	87.5
Syphilis	14	58.3	10	41.7	0	0.0	10	41.7	14	58.3
Urine analysis	22	91.7	2	8.3	0	0.0	13	54.2	11	45.8
Stool analysis	3	12.5	3	12.5	18	75.0	4	16.7	0	0.0
Ultrasound	4	16.7	6	25.0	14	58.3	10	41.7	0	0.0

Current practice and opinion regarding diabetes screening during pregnancy

In private facilities, blood glucose was checked always in three (25.0%), rarely in four (33%) and not done in five (41.7%) (Table 6.4). In the government facilities, blood was tested for glucose rarely in nine HFs (75%) and three facilities did not perform the test at all. In the HFs where blood glucose test was performed, it was always done regardless of the last meal and using portable glucometer; oral glucose tolerance tests were seldomly done. Every positive case found was referred to the gynaecologist within the same HF, to the district hospital or to the diabetes clinic. A total of 13 HFs (54%) reported to selectively carry out blood glucose testing to women with glycosuria or those with obvious clinical symptoms of hyperglycaemia. However eight HFs (33.3%) reported to never have found any glycosuria.

Table 6.4: Blood glucose testing during pregnancy: Comparison of surveyed government and private HFs

Variable		Government (n=12)		Private (n=12)	
		N	%	n	%
Blood glucose tested	Always	0	0.0	3	25.0
	Rarely	9	75.0	4	33.3
	Never	3	25.0	5	41.7
Type of test (for those who do the test)	Universal	0	0.0	3	42.9
	Selective	9	100	4	33.3
Testing procedure	Random BG	9	100	7	100
Device used	Portable glucometer	6	66.7	7	100
	Laboratory	3	33.3	0	0.0
Paying for the test	Yes	2	22.2	7	100
	No	7	77.7	0	0.0

Health workers liked the idea of blood screening for GDM but they mentioned that this would include several changes in the ANC protocol, and hence modification of ANC cards and training of care providers. Also, the government should commit to supply the glucometers and strips. In addition, some health care providers, especially those working at the district hospitals, expressed their concern that even the current protocol is not implemented properly. In most cases supplements, test kits and reagents are out of stock, so they were not sure how the introduction of a new item could be implemented unless there is donor support like for HIV/PMTCT interventions. One of the health workers from a government dispensary said "*Blood from the mothers is drawn anyway for the syphilis and HIV tests, so it is easy to incorporate blood glucose test within that context. However, protocol and logistic supplies are very important".*

Another statement from a health worker in one of the government hospitals that explained the possible challenges was *"Even the current ANC protocol (FANC) is not*

followed due to shortage of resources including personnel, I am worried if introduction of another item which will cost more time and personnel can work"

Generally, there were mixed views with regard to blood glucose testing. While few health care workers felt that the current practice of glucose test in urine is enough the majority suggested that blood glucose test can be done with minimum additional cost

The private hospitals charge a fee for most ANC services, except for PMTCT and micronutrient supplements which are provided by the government. The cost for a blood glucose test ranged from 1500 to 6000 Tanzanian shillings which is equivalent to about 1 to 4 USD per test (Table 6.4). Except in few private hospitals where a woman will be directly attended by a gynaecologist, in most cases the nurses were handling all women during ANC visit and referred them either to see the clinical officer in-charge of RCH, the gynaecologist, the health centre or to the district hospital depending on the complication(s)/pregnancy danger sign a woman has. The most common reported causes of referral included anaemia (Hb<8.5g/dl), hypertension, oedema/preeclampsia, mal-presentation, previous scar, under-age, malaria, multiple pregnancy, urinary tract infections, negative Rhesus factor, bleeding, lower abdominal pain and sometimes low stature (height <150cm) (Table 6.5).

Table 6.5: Reasons for referring pregnant woman to the specialist

Reason for referral	N	%
Low Hb (<7 g/dl)	17	70.8
PIH	19	79.2
malposition	15	62.5
Previous stillbirth	13	54.2
Sugar in urine	16	66.7
Severe malaria	15	65.5
History of caesarean	12	50.0
Prolonged labour	12	50
Negative RH factor	23	95.8

Hb: Haemoglobin, PIH: pregnancy induced hypertension, RH: Rhesus factor

When asked about the kind of training received in the past five years, most RCH care providers attended training on HIV/PMTCT (95.8%), family planning (75.0%), FANC (66.7%), preeclampsia (66.7%).Less were trained on trained on nutrition (41.7%), and diabetes (16.7%).

Discussion

This study sought to summarise available literature on ANC in Tanzania and to assess possibilities of blood glucose testing for GDM during ANC visit. In our study, immunization, family planning, PMTCT and health education and counselling were regularly performed in almost all surveyed HFs. More than 90% of the HFs did urine analysis for glucose, albumin and leucocytes regularly and those with positive glycosuria were referred to district hospital or to the diabetes clinic.

Similar with what was observed in the studies in rural areas [26, 27], some of the recommended test were not done in the urban setting. This was similar to what was reported in another study that there was inadequate infrastructure, equipment and supplies for perinatal care in Dar es Salaam public health institutions [37]. Other researchers reported poor quality of care in ANC in both private and government HFs in Dar es Salaam, but the private facilities were relatively performing better [38]. However, only few women can attend private HFs. In the rural area, urine testing for albumin and glucose was rarely done in most of the clinics [33]. Some clinics reported to have never found any woman with glycosuria, probably due to low sensitivity of urine test to identify GDM cases. In our previous study, most women with GDM had normal urine test for glucose [5], hence if screening is based on urine analysis instead of blood glucose test, most women will be left undiagnosed.

Blood glucose test was done in few private HFs and the cost is considered high to an ordinary pregnant woman in Tanzania, but perhaps it is because these are profit making organisations. In reality, the actual cost for screening alone may be lower, but total cost for treatment, care and increased number of ANC visits may be high. Increased costs for care in women diagnosed with GDM was reported elsewhere [39]. Another issue may be the psychological impact for those who would be diagnosed with GDM due social stigma or fear of having a lifelong disease [40, 41].

Opportunities for blood glucose testing during ANC visit

As commented by the respondents and based on the reports in literature, there are good opportunities for including diabetes screening in the usual RCH regimen. One of the opportunities is the existing screening for HIV and syphilis during ANC visit. In Tanzania, syphilis and HIV screening is a mandatory part of routine ANC. This is a good opportunity since blood is already drawn within the ANC and not in the central laboratories as it is done for other biochemical tests. Another opportunity is the existence of health/nutrition education and counselling for danger signs which could be utilized by adding a component of GDM as one of the danger signs. Although in most cases counselling is done in groups, it is still worth to train health care providers so that proper counselling to at risk individuals can be done during regular ANC counselling sessions.

Several contacts to the RCH clinic including prenatal, postnatal and child care programmes would as well provide close follow-up of women with GDM or those with risk factors. According to the demographic and health survey of 2010, 96% of pregnant women had at least one visit, and there is good coverage for ANC as about 80% of the women live within 5km from ANC [3]. Overall, only half of the pregnant women gave birth at the health facility but variation between rural and urban areas was large, with 42% in the rural areas and more than 80% in the urban area. High institutional delivery especially in urban areas is an opportunity such that women identified or those who could have been missed during ANC can still be assessed for GDM during delivery. Moreover, there is a good organized referral system whereby district and regional hospitals are located in almost all districts and all regions respectively, which are better equipped and with more specialised doctors. Likewise, there are also established diabetic clinics to handle diabetes cases in almost every region and in most of the districts.

The inclusion of urine tests for albumin and glucose as mandatory requirement for all pregnant women attending ANC shows that the danger of diabetes during pregnancy is already recognised by the government.

Challenges

Next to the mentioned opportunities, there are also challenges which need to be addressed. Some were identified during the survey and others were reported in the reviewed literature. Limited human and materials resource were mostly reported among the factors affecting quality of ANC. These are also the two main recognized problems in Tanzanian health care [16].

Furthermore, the few present staff in ANC lacks several skills with regard to counselling and management of aspects related to pregnancy. In our study, most RCH care providers received in-service training on HIV/PMTCT, family planning, FANC and tuberculosis which could probably be due to donor support of the integrated management of childhood illness (IMCI) FANC and Safe Motherhood programmes. Training on diabetes was however rare. Management and counselling of women diagnosed with GDM is important, hence health care providers should be trained in proper education and counselling skills. In the urban Tanzanian region, the average time spent for the ANC visit is 15 and 9 minutes for the first and subsequent visits respectively [42]. In the rural Tanzania district, Pembe et al. reported deficiencies in counselling on danger signs during pregnancy and observed inadequate time for interaction between antenatal care providers and their clients [28]. The addition of another component which may need extra time for counselling may bring extra work load to the already overburdened health care providers, especially in settings with limited ANC providers.

Another challenge is the cost. Lack of money was reported as one of the factors affecting number of ANC visits [35]. In our study, we found that testing blood glucose levels may be unaffordable for an ordinary Tanzanian woman if it will be implemented without government support. However, this was in private clinics which are mainly profit oriented. In the government clinics, the primary costs for screening and diagnosis would be for the glucometer and the strips, which in that case may be low. However, the subsequent cost for management and treatment may be high [43]. The free access to exemption policy for ANC services is sometimes not applicable since mothers have to pay in private laboratories for check-ups done during ANC like urine tests and testing of blood group and Hb levels. We speculate that, women at risk may be willing to pay for the extra costs for GDM testing and treatment if they are informed well and their partners are involved. However, a well-planned study to assess additional costs and willingness to pay is needed to support such a policy.

With regard to screening and diagnosis guidelines, there is no guideline for blood glucose testing during ANC in Tanzania. A recent training manual for non-communicable diseases has a component of GDM and it recommends universal screening for all pregnant women aged above 30 years and selectively for those at risk [44]. The ANC card for recording all the assessments has been used as a guide for ANC services. Gross et al [31] found that some aspects recommended by FANC were missing in ANC cards and this was probably one of the reasons for not following all FANC procedures by some of the health care providers. In case GDM has to be included, there is a need to change the format of the existing ANC cards.

Concluding remarks

This review and HF survey describe existing health care with respect to ANC in Tanzania together with a discussion on possible opportunities and challenges for inclusion of GDM screening during ANC services. Our HF survey included 10% of the HFs offering ANC in Dar es Salaam city hence representativeness of the results to other regions in the country cannot be ascertained. Diabetes screening during pregnancy is already in place in most of the ANC in Dar es Salaam region. Urine test for glucose is part of the general ANC guideline. However, in rural areas it is seldomly done. While working on the existing challenges, blood glucose testing using the existing HIV/PMTCT as an entry point is suggested.

Some argue that universal screening is more relevant as it detects more cases and may improve diagnosis and care, and eventually improve the outcome [45, 46]. In addition, those who advocate for universal screening also argue that some women (up to 30%) may be missed with selective screening and there are no additional cost when universal screening is compared with selective screening [45, 47]. On the other hand, treatment and management has only be proven to be effective among women with risk factors, thus emphasis selective screening [48]. Due to limited resources, selective screening based on risk factors would be more realistic in our setting. In that case, there is a need to develop scores relevant to the Tanzanian situation which can be used to easily identify women at risk. In addition, the ANC should be prepared for treating, counselling and regular follow-up of the identified GDM cases. As an alternative, women at risk can be identified using a risk score without blood glucose testing, and counselled for lifestyle modification to avoid adverse outcomes.

Our results show that it is also important to improve awareness amongst healthcare providers at all levels. In addition, the mind set of obstetricians need also to be geared towards having an index of suspicion for those who may have

GDM. Setting-up guidelines, training and acquiring resources should start, and meanwhile further studies on the costs and benefits need to be done to justify blood glucose testing for screening in Tanzania especially in the urban areas where prevalence was relatively high.

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Chapter 7

General discussion

The main focus of this thesis was to determine the prevalence of gestational diabetes mellitus (GDM) and its determinants in urban and rural areas in Tanzania and in Sub Saharan Africa (SSA). Five specific study questions were formulated (**Chapter 1**) and investigated in chapters 2 to 6. A total of 910 pregnant women attending antenatal clinics (ANC) in selected rural and urban areas were invited to participate. In this chapter the main findings are summarised followed by a discussion on methodological considerations and the public health relevance. Finally, suggestions for future research are given.

The key findings are summarised below and in Table 7.1. The prevalence of GDM in Tanzania was high, with a much higher prevalence in urban compared to rural areas (**Chapter 2**). Risk factors associated with GDM were family history of diabetes, previous stillbirth, mid upper arm circumference (MUAC) ≥28cm overweight or obesity and anaemia. No significant association of other factors such as maternal height, age, gestational age or dietary diversity with GDM was observed.

We identified 22 studies reporting the prevalence and or risk factors of GDM in six SSA countries (**Chapter 3**). Heterogeneity in the 15 studies with low or moderate risk of bias, that were included in a meta-regression analysis, was high. We observed a relatively higher prevalence in studies done after the year 2000 compared to studies done before 2000 (5.1% vs 3.7%), when women at risk were examined compared to less risk (6.5% vs 3.8%) and when more current diagnostic criteria were used compared to older ones (5.11%vs 4.25%). In the studies conducted after the year 2000, the prevalence of GDM ranged from 0.3% (95% CI 0.2-0.5) in a tertiary university hospital to 13.9% (95% CI 11.5-16.4) in a high risk population in Nigeria. When categorized into sub-regions, the prevalence proportion estimates were similar in West, East and South African studies **(**Table 3.2**)**. Six risk factors were reported in more than one study, namely advanced maternal age (≥30 years), overweight and obesity, previous macrosomic child, previous still birth, family history of type 2 diabetes and history of GDM. While definitions of other reported risk factors were similar, the definition for overweight or obesity was different in each study where by MUAC, body weight or BMI were used.

The prevalence of hypertensive disorders of pregnancy (HDP) in the current study was 8.9% in the urban areas and 5.3% in the rural areas (**Chapter 4**). Advanced maternal age, high gestational age, increased MUAC, increased dietary diversity and being HIV positive were independently associated with HDP in urban women. Increased age and gestational age were identified as independent risk factors in rural women. We did not find a clear association between GDM and HDP.

Regarding the birth outcomes in the urban population, occurrence of macrosomia was higher than that of low birth weight (**Chapter 5**). We observed high occurrence of macrosomia in single compared to married women (11.0% vs 4.9%) and less occurrence among self-employed compared to unemployed (3.4% vs 9.0%). GDM and birth weight of the previous child were significantly associated with macrosomia, after adjustment for confounders, while presence of HDP was the main predictor of low birth weight. Other factors such as HIV status, anaemia, maternal height, education level and gestational age at first visit to the clinic were not associated with birth weight in our study population.

We identified several challenges in the antenatal care system in Tanzania; the main ones being limited material and human resources (**Chapter 6**). The regular contacts of the pregnant women with the health care, HIV testing and the existing counselling services provide an opportunity for including selective blood glucose testing during antenatal care (ANC) visits.

Table 7.1: Summary of the main findings of studies described in this thesis

Study population, setting, sample size and design	Main findings
• Research question: *Is gestational diabetes mellitus present in Tanzania? If yes, what are the determinants?* ***(Chapter 2)***	
Pregnant women (N=910); urban (n=609) and rural (n = 301); cross sectional survey	• Overall prevalence of GDM was 5.9%. • Higher prevalence in urban (8.4%) compared to rural areas (1.0%) • Associated risk factors include MUAC ≥28cm, previous stillbirth, anaemia and family history of diabetes
• Research question: *What is the burden and risk factors for gestational diabetes mellitus in Sub-Saharan Africa?* ***(Chapter 3)***	
Systematic review and meta regression analysis of gestational diabetes in SSA. Published journal articles in PubMed, manual search for identified potential articles from reference list	• Few studies (n=22) from six SSA countries. • High heterogeneity among studies with low or moderate risk of bias(n=15) • Highest prevalence was up to 13.9% among high risk women • General trend shows increased prevalence in studies done after the year 2000
• Research question: *What is the prevalence and potential risk factor(s) for hypertension during pregnancy in women attending antenatal clinics in Tanzania?* ***(Chapter 4)***	
Pregnant women (N=910); urban (n=609) and rural (n = 301); cross sectional survey	• Overall prevalence of hypertension during pregnancy was 7.7%; higher prevalence in urban areas (8.9%) compared to rural areas (5.3%) • Associated risk factors: ○ urban areas: age, gestational age, MUAC, HIV and dietary diversity score ○ Rural areas: age and gestational age
• Research question: *What are the maternal risk factors for macrosomia and low birth weight?* ***(Chapter 5)***	
Urban women (n=466); prospective cohort	• Occurrence of macrosomia and low birth weight were 5.9% and 3.6% respectively. • GDM and previous macrosomic infant were associated with macrosomia • HDP was associated with low birth weight and stillbirth

• Research question: *How is the Tanzania antenatal care system prepared to handle the rising challenge of diabetes in pregnancy? (**Chapter 6**) OR can blood glucose testing be integrated in the usual ANC services?*	
Literature review, urban health facilities survey (n=12 private and n=12 government facilities)	• Diabetes screening using urine test for glucose is universally done in the urban area • The main challenge is limited human and material resources • Existing HIV counselling and testing can be used as an entry point for blood glucose testing with minor adjustment and training • Further studies on costs for screening and management are needed

Methodological aspects

Although methodological considerations were discussed in each chapter, this section will elaborate on issues to take into account when interpreting the findings or applying the methods used in this thesis in a different setting. The potential sources of error discussed possibly affect internal validity, are classified into selection bias, information bias and confounding [1].

Selection of study participants

Generally, selection bias may occur during enrolment or due to decline to participate or loss to follow-up. Our study was done in a rural and urban antenatal clinic setting where women attending antenatal care were invited and consented to participate (**Chapter 2, 4, & 5**).the majority of the Tanzanian women (96%) attend ANC at least once during pregnancy [2].

In urban areas, 715 women were invited to participate, 637 qualified for examination and 599 completed OGTT. In the rural areas, 400 eligible women were invited to participate, 315 qualified for examination and 301 completed OGTT. Overall response rates were 89% and 79% in urban and rural areas respectively (**Chapter 2 & 4**). Loss to follow-up in the urban area was about 23% (**Chapter 5**). Based on the high ANC attendance rate and high response rates our study population can be seen as representative of the majority of the pregnant women in the studied areas.

One of the inclusion criteria was pregnant women who were ≥20 years old during recruitment. We considered this age category to match the characteristics of rural

and urban women. According to Tanzania Demographic and Health Surveys (TDHS) (2010) [2], teenage pregnancy is relatively higher in rural (26%) compared to urban areas (15%), hence inclusion of teenage women would have resulted in a wider variation in the characteristics of the participants, but also more difficulties in in comparing the urban and rural areas. In addition, prevalence of GDM increases with age so it is less likely to find teenage women with GDM. We also limited our inclusion to women at gestational age ≥20 weeks, as placental hormones that affect glucose metabolism start increasing considerably at the second and third trimester [3]. The usual initiation of antenatal clinic attendance in Tanzania was also considered, which was around five months [2]. Most guidelines consider GDM screening at 24 to 28 gestational weeks and earlier for high risk women [4, 5]. Nevertheless, when stratified according to gestational age (<24 weeks, 25 to 29 weeks and above ≥30 weeks), we observed no differences in mean blood glucose levels or mean MUAC between these three gestational age categories (**Chapter 2**).

Information or misclassification bias

Error in measuring exposure or outcome may cause information bias. The outcomes studied in this thesis include prevalence of GDM (**Chapter 2**), prevalence of HDP (**Chapter 4**) and birth weight (**Chapter 5**). Error in the prevalence estimate of GDM may occur if participants are classified as having GDM while they are not. To minimize this error, all women were categorised as having GDM or not based on a standard, the WHO 1999 criteria. It is recommended that the best way to diagnose GDM is the use of oral glucose tolerance test (OGTT) [6]. Nevertheless, ten women who did not undergo the OGTT were included (Table 2.4). Among them, eight women were diagnosed using two fasting blood glucose measurements ≥6.1 mmol/L and two women by using fasting blood glucose ≥6.1mmol/L in combination with random blood glucose ≥7.8mmol/L. Blood glucose was measured using HemoCue glucose analyser. This portable glucometer is considered to be reliable and accurate for both fasting and OGTT glucose levels, and comparable to other accurate laboratory methods [7, 8].

The definition of hypertensive disorders of pregnancy includes women with chronic hypertension, preeclampsia or pregnancy induced hypertension without preeclampsia [9, 10]. In this study, women were classified as being hypertensive during pregnancy if systolic blood pressure was ≥140mmHg or diastolic blood pressure ≥90mmHg regardless of the subtypes. In Tanzania, blood pressure is monitored during each ANC visit and the ANC guideline requires all women with

blood pressure ≥140/90mmHg to be referred to the medical doctor for further investigations and management. It is recommended that blood pressure measurements be repeated within the same week in another day [11, 12]. This was not possible in our setting so the true prevalence might be overestimated. Blood pressure measurements can be subject to bias due to cuff size relative to the arm, arm position or equipment used [13]. Measurements were taken by an experienced midwife and the automated device used was checked regularly.

A child is classified correctly at birth into preterm, term or post term based on gestational age. According to WHO, low birth weight is defined as weight at birth of <2500 g and it includes preterm births, small for gestation i.e. <10th percentile, or born term but small [14]. In our study (**Chapter 4**), infants were classified into low birth weight or macrosomia if they were born within 37 to 42 gestation weeks.

Accurate estimation of gestational age is essential for correctly classifying infants according to birth weight. Gestational age was extracted from ANC card. Although ultrasound is considered more accurate, in Tanzanian ANC the common method used for estimation of gestational age is based on the last menstrual period reported by the mother during first visit [15, 16]. Estimating gestational age by recall may be prone to some error because some women may have irregular menstrual cycle [17].

With regard to macrosomia, there is no universally accepted definition [18]. It varies from birth weight ≥4000 g to ≥4500 g, or the 90, 95 or 97 percentile of the population specific growth curve. In SSA the 90th percentiles of birth weight ranged from 3600 g in Niger to 4050 g in Algeria [19]. In our case, cut off of ≥4000 g was used.

A source of error could be late weighing of the infant. It is recommended that birth weight should be measured within four hours after delivery [14]. As all women reported to have delivered in a health facility, we are convinced that infants were measured within the recommended duration.

Error in the assessment of exposure variables

Overweight and obesity: In general women are classified as overweight or obese using pre-gestational weight or weight measured during first visit if before 12 gestational weeks. Only less than half of the women could recall their pre-gestational weight and most of them started attending to the clinic late (gestational age at booking ranged 8-32 weeks with a mean of 20 weeks). We therefore used MUAC as a proxy for BMI. MUAC is known to be relatively stable during the course of pregnancy and it was highly correlated with pre-pregnancy BMI [20-22]. In our

study population MUAC and BMI at booking were correlated at r=0.78. In addition, we used receiver operating curve (ROC) analysis to assess the sensitivity and specificity of MUAC as a predictor of GDM and HDP as shown in Figure 7.1. The results of the ROC analysis showed that for GDM the area under the curve was 0.56 (95% CI 0.48 – 0.64). The optimal cut-off point (the point that maximize sensitivity + specificity i.e. Youden Index J) for detecting GDM was 28.4 cm with sensitivity of 0.46 and specificity of 0.70 (1-specificy = 0.30). This means that relying on a MUAC cut-off of 28 cm alone, only 46% of women with GDM will be correctly identified and 30% of women without GDM will have positive results. Considering HDP as the outcome, the area under the curve was higher, 0.65 (95% CI 0.58 - 0.72), with optimal cut-off point of 29.0cm; sensitivity was 0.50 and specificity is 0.78. This means relying on MUAC cut-off of 29 cm alone, only half of women with HDP will be correctly identified and 22% of women without HDP will receive positive results. Although it has rather low sensitivity for GDM and HDP, MUAC can be used to identify overweight/obese women during ANC visits so that they can be counselled for recommended pregnancy weight gain and monitored for GDM and HDP.

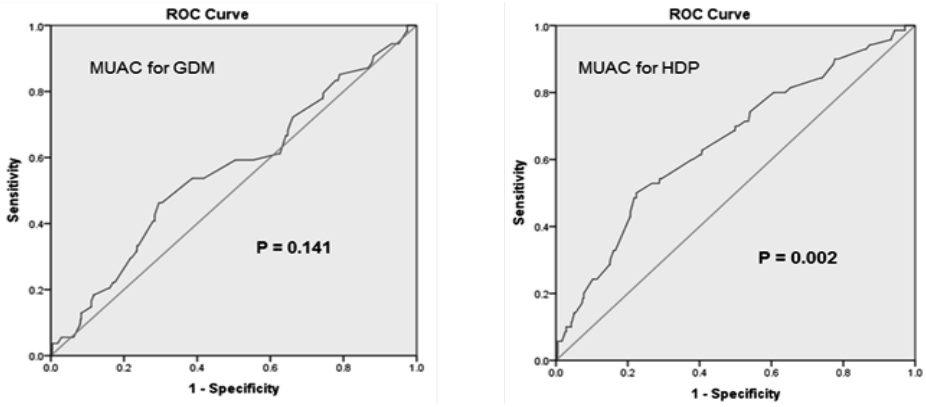

Figure 7.1 ROC to assess for MUAC as a predictor for GDM and HDP

Dietary diversity score: Dietary intake assessment was based on data collected using the 24-hour recall method. Foods consumed were assigned into pre-determined food groups and a dietary diversity score was obtained by summing up the food groups consumed [23]. The FAO questionnaire has 16 food groups which are then aggregated to 9 food groups in assessing dietary adequacy for women [23]. We used all 16 food groups to capture micronutrient intake as well as consumption of sweets and beverages which are known to be associated with the

metabolic syndrome. In this method, each food group is assigned equal value irrespective of its health effect or nutritional quality.
Recall bias is common in dietary recall methods and sometimes foods consumed outside home are forgotten [24]. This bias was minimised by using trained interviewers prompting for such occasions. Although a single 24-hour recall was thought to be sufficient [25], bias due to day-to-day variation of consumption cannot be ruled out completely. Up to seven days recall period was recommended and thought to be sufficient to minimize memory error [26]. In future, pre-pregnancy dietary intake or dietary pattern analysis should be considered since they represent a broader picture of food and nutrient intake and may be a better predictor of disease risk [27, 28].
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Physical activity: We assessed physical activity using the short form of the international physical activity questionnaire (IPAQ) which reports Metabolic equivalents (MET-minutes/week).Although an objective measure of physical activities during pregnancy is mostly recommended [29], wearing a pedometer or accelerometer may also affect the usual activity pattern. The device may also fail to record some activities for example, if it is put on the lower part of the body, the activities involving the upper part of the body like weight lifting or carying a load will not be recorded [30]. The method used was therefore considered appropriate and more practical for our setting.

In this thesis, much higher METS-minutes per week in rural compared to urban women were observed, showing that the method may have satisfactorily classified women correctly into low, moderate or high level of physical activities per week. In future, other questionnaire based methods should be explored in comparison with the use of objective assessment of physical activities in pregnant SSA women.

Anaemia: Haemoglobin (Hb) concentrations were measured using HemoCue Hb 201+ Haemoglobin photometer. This is one of the recommended equipment for measuring Hb levels [31]. To minimize systematic error, the glucometer was checked every day as recommended by the manufacturer. Anaemia was defined as Hb<11 g/dl [32]. Prevalence of anaemia in our study population was about 70%. Haemodilution that occurs during the second and third trimesters as well as altitude and smoking status may affect Hb concentrations in pregnant women [32]. We observed a similar prevalence of anaemia across gestational age; our study was done in the low land (≤1000 m above sea level) and smoking was not common in the study areas. Hb is always used as a proxy for iron deficiency anaemia during

pregnancy. It is estimated that majority of the low Hb levels in developing countries would be due to iron deficiency [31]. However, the use of serum ferritin was recommended to give better insight in prevalence of iron deficiency anaemia [33]. High levels of infection and inflammation may limit the use of serum ferritin as a biomarker for iron deficiency in SSA. [32]. Use of other biomarkers such as hepcidin and C-reactive protein in GDM should be further explored.

Confounding

Another possible source of error that can affect internal validity is confounding. Confounding occurs when a measure of association or relationship between exposure and outcome is distorted due to the presence of a third variable, a confounder [34]. For example, from the literature, overweight or obesity and increased maternal age are known risk factors for GDM. Older women are also at higher risk for being overweight or obese. The association of overweight or obesity with GDM may therefore be confounded by age. Possible confounders reported in the literature were adjusted for in chapters 2, 4 & 5. However, due to the observational nature of our study, bias attributable to unmeasured (for example vitamin D and iron status, malaria, syphilis, socioeconomic status) or unknown confounders cannot be ruled out.

Public health implication of the findings

GDM is increasingly common in Tanzania and in SSA and is associated with increased risk of foetal macrosomia (**Chapter 2, 3 & 5**). In addition, the prevalence of HDP is high and it is associated with low birth weight and still births (**Chapter 4 &5**). Thus, GDM and HDP during pregnancy pose a major public health challenge to the ill-equipped health system (**Chapter 6**). The much higher prevalence of GDM and HDP in urban compared to the rural areas implies that lifestyle plays a role in their occurrence.

Although we did not find differences in MUAC among rural and urban women, the active lifestyle of rural women could be protective since the majority of them were engaged in agricultural work, hence had higher level of physical activities [35-37]. In addition, urban women had more diversified diet (**Chapter 4**) which is a reflection of their socioeconomic status. Like many other developing countries, changes in the food consumption pattern in SSA together with urbanisation have resulted in an increased prevalence of overweight and obesity. Lifestyle interventions targeting women of reproductive age to maintain normal body weight before conception, such as a healthy diet and regular physical exercise, may reduce the risk for GDM [38-40]. Planning intervention for women at risk will not only reduce

the risk of GDM but also for other metabolic complications associated with overweight and obesity.

Diagnosis

Worldwide, there are variations in screening methods and diagnostic criteria used for GDM. Some guidelines recommend two steps, the first step including a screening test with 50 g of glucose and the second one involving 100 g OGTT while others recommend one step using the 75 g OGTT (**Chapter 1**). Moreover, to recommend universal or selective screening, together with gestational age to start screening, is still a topic of debate. The new guideline of WHO 2013 [5] recommends diagnosis of GDM using 2 hr 75 g OGTT with a cut-off for fasting blood glucose of 5.1mmol/L, which is a lower cut-off as compared to WHO 1999 guideline which we used in our study. Due to variation in prevalence rates reported when different criteria are used in the same population, there have been always difficulties in comparing prevalence rates between different countries, so if implemented generally, it will make comparison of epidemiological studies in SSA easier. On the other hand, due to the lower cut-off for fasting glucose levels, more cases will be identified, where perhaps some of them will not benefit from the treatment [41]. For example, in our study, the prevalence of GDM was more than double (13.0%, CI 11.4-15.4) when IADPSG [42] criteria which is similar to the new WHO 2013 guideline was used [5]. In Nigeria, screening based on a checklist of risk factors was found to be more effective than universal screening [43]. Considering selective screening based on risk factors, if we would have screened pregnant women based on the six risk factors (MUAC ≥ 28cm, family history of diabetes, previous stillbirth, age ≥30 years and previous macrosomic child); four out of five women would have at least one of the risk factors; but about 15% of the GDM cases would be remained undiagnosed. Other studies that used different selection criteria found that up to 30% GDM cases would be missed with selective screening [44].

Another aspect to consider is the need for OGTT for diagnosis. In most of the developing countries, OGTT may be challenging due to limited staff and logistical issues, and some women may fail to tolerate it. Other options like the use of fasting or random blood glucose could be more practical and cost-effective in this setting; however, there is a need for further exploration of this issue. Resource limited countries may need to set their own criteria, depending on the availability of resources [45].

Treatment options

Treating GDM is aimed at achieving glycaemic control to reduce preeclampsia, shoulder dystocia and macrosomia [46]. The commonly used treatment is dietary modification and physical activity together with blood glucose monitoring. Sometimes oral anti-diabetic agents or insulin may be used, depending on the severity [47]. In developing countries, insulin may be un-affordable to most pregnant women, hence oral hypoglycaemic agents such as metformin could be an alternative [48-50]. However, taking medication without a clear understanding may reduce compliance, so proper knowledge about the glucose intolerance state should be communicated to the mother. This calls for specific training of the health care providers especially those dealing with maternal and child health.

Prevention

Due to increased risk of metabolic syndrome in women with GDM, interventions should target both prevention of GDM and prevention of progression to type 2 diabetes [51].There are limited intervention studies for reducing overweight or obesity in SSA, the main focus has been on undernutrition. A systematic review on interventions for preventing GDM showed that dietary counselling and low glycaemic index diets may have some benefits in preventing GDM [52]. Likewise, postpartum lifestyle interventions on diet, physical activities and weight reduction were shown to improve diabetes risk factors in women with GDM [53]. In our studies, overweight or obesity was associated with increased risk of GDM and HDP after adjustment for potential confounders such as age and gestational age (**Chapter 2 &4**). In the African context, weight reduction programmes or controlling weight gain during pregnancy may be a challenge due to cultural aspects of obesity in women [54, 55]. Obesity is regarded as beauty and perceived as a sign of prosperity, while slimness is viewed as unhealthy or sign of diseases. Dietary counselling may require women to change their usual diets in order to control blood glucose levels, which may fail due to lack of compliance. Public awareness is therefore very important in this setting. Also, targeting women at a younger age may be more beneficial than after conception or after delivery [56].

In observational studies, a higher level of physical activities before or during pregnancy was associated with a reduced risk of GDM [37] but intervention studies for prevention of GDM were less effective as compared to interventions for GDM management [57, 58]. The main reason given for failure of physical activity

interventions to prevent GDM may be compliance. Rural women are usually physically active due to the nature of their daily activities. In urban SSA, lifestyle and logistics do not allow recommended physical activity level for pregnant women which, in order to be effective, should include a walk at vigorous intensity for 25 minutes per session or at least 35 minutes per session at a low intensity, together with a modified diet [59].

Another aspect considered for reducing progression to type 2 diabetes is breast feeding. In a review of observational and prospective studies, breast feeding was associated with improved glucose and lipid metabolism and reduced risk of type 2 diabetes in women with GDM [60]. Breastfeeding may also be beneficial in preventing childhood and future obesity depending on the duration [61, 62]. In SSA, breast feeding is regarded as essential for every woman and duration is generally high, but exclusive breast feeding for the first six months is low [2, 63].

Most of the studies reported that high haemoglobin levels and high serum ferritin levels were associated with increased risk of GDM [64, 65]. In our study, we found that GDM was more prevalent in anaemic women compared to women with normal Hb levels (**Chapter 2**). Hb levels have been used as a proxy for iron deficiency anemia and as a guide for supplementation during antenatal care. The main cause of anaemia in most SSA countries is iron deficiency due to low dietary intake, but infections such as malaria and HIV, parasites, and vitamin A deficiency also contribute to anaemia during pregnancy [31, 66]. The interventions in place for prevention of anaemia during pregnancy include malaria treatment and prophylaxis, subsidised mosquito insecticide treated bed-nets, deworming and iron supplimentation. Iron overload due to supplimentation has not been reported, hence reinforcing the interventions to inrease Hb levels may also reduce the risk of GDM. Although high serum ferritin level was considered a risk for GDM [64, 67], randomized trials showed that iron supplimentation does not increase the risk of GDM [68, 69]. In women who were not anaemic and with risk factors for GDM, it was suggested that high iron intake may increase the risk for GDM [70]. There is limited studies on the effect of iron supplementation on glucose intolerance during pregnancy in SSA.

Suggestion for future research

In view of our findings, the following suggestions for future research can be made:

- Short and long term prospective studies are needed to evaluate the range of factors associated with GDM and birth outcomes in SSA. Attention should be given to pre-and post-gestational risk factors (such as MUAC, body fat, inflammation markers, waist circumference) that determine progression of type 2 diabetes, the effect on the child, recurrence of GDM in successive pregnancies and possible ways of reducing the risks.
- Although women with GDM may return to normal after delivery, they may confuse their condition with type 2 diabetes if not properly counselled. It is therefore important to explore psychological effects in women diagnosed with GDM in Tanzania which will guide in planning for tailored counselling.
- Studies on cost-benefit analysis for either universal or selective screening in SSA are needed and should include assessment of the extra costs for treatment, extra visits to ANC and general management of women diagnosed with GDM.
- In the SSA setting, shortage of staff and limited resources is common in ANC. Diagnosis of GDM using OGTT may, therefore, be challenging. To implement selective screening, possible risk factors need to be explored. The existing challenges of OGTT as a diagnostic test call for further studies to establish easier and cost-effective way of diagnosis of GDM in the region.
- Behaviour change for lowering blood glucose and preventing progression from GDM to type 2 diabetes depends on individual knowledge and attitudes. Qualitative studies focusing on women's perception after diagnosis and their attitude towards behaviour change are lacking in SSA.
- We observed that overweight/obesity was associated with increased risk for GDM and HDP. Behaviour change interventions to reduce overweight/obesity targeting women before conception should be given priority in SSA
- There was high prevalence of anaemia in our study population, possibly due to the fact that the two study areas are malaria endemic. We recommend further studies to explore the co-existence of infection and GDM as well as the effect (if any) of iron supplementation on glucose intolerance during pregnancy in SSA.

Conclusion

This is the first study that has assessed the burden of GDM and its determinants in Tanzania since 1990 and in SSA and explored the possibility of integrating blood glucose testing in the usual ANC in Tanzania. Gestational diabetes mellitus in Tanzania is increasing in parallel to the increasing prevalence of obesity and type 2 diabetes mellitus. The association of overweight and obesity with both GDM and HDP provide an insight in the importance of weight reduction interventions. Strategies to prevent overweight and obesity before pregnancy will result in reduction of GDM and HDP and hence prevent intergenerational transmission of these chronic disorders. Proper utilization of available resources to include selective blood glucose testing during ANC visits is necessary and should be implemented together with lifestyle counselling.

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Summary

The prevalence of overweight/obesity and type 2 diabetes is increasing in most of the Sub Sahara African (SSA) countries. The commonly given explanation for the observed increase is the change in lifestyle, such as food consumption and activity pattern, mainly due to urbanisation. Gestational diabetes mellitus (GDM) has been recognized as a potential risk factor for future type 2 diabetes to the foetus and the mother. Early identification and management reduce the risk of adverse outcomes, hence understanding the burden of GDM and its risk factors is important for better planning of preventive interventions to break the intergeneration cycle for type 2 diabetes.

This thesis aimed to determine the prevalence of gestational diabetes mellitus (GDM) and its determinants in urban and rural areas in Tanzania and in Sub Saharan Africa (SSA).

We first assessed the prevalence and risk factors for GDM in Tanzania, comparing rural and urban areas (**Chapter 2**). This was achieved through a cross-sectional survey in selected antenatal care facilities where women attending clinic were requested to participate. We noted a higher prevalence of GDM in urban areas (8.4%) compared to rural (1.0%) areas, with an overall prevalence of 5.9%, which was much higher compared to what was reported in the 1990s. A possible explanation of the rural versus urban differences could be the nature of physical activity level as most of the rural women are engaged in agricultural work, which is more energy intensive. Family history of type 2 diabetes, overweight/obesity a defined as mid upper arm circumference (MUAC) ≥28 cm and previous stillbirth were significantly associated with presence of GDM. A higher prevalence was also observed among women with anaemia compared to those with normal haemoglobin levels. It is important to note that the prevalence varied according to the diagnostic criteria used; when using the diagnostic criteria recommended by the International Association of Diabetes in Pregnancy Study Group (IADPSG) with a lower cut-off for fasting glucose levels, the prevalence of GDM was more than double (13.0%).

The burden of GDM and its risk factors in SSA was assessed through a systematic review and meta-regression analysis of published literature (**Chapter 3**). We retrieved only 22 studies conducted in six out of the 47 SSA countries, most of them from Nigeria. We found high heterogeneity between the studies, which could not be explained by any of the variables in a meta-regression analysis. Prevalence was up to 14% when high-risk women were studied. Commonly reported risk

factors were overweight and/or obesity, family history for type 2 diabetes, GDM in previous pregnancy, previous still birth, previous macrosomic child and age >30 years.

In **Chapter 4**, we assessed the prevalence of hypertension during pregnancy (HDP), which is another risk factor for delivery complications. During pregnancy, GDM and HDP often occur together. Although blood pressure is always measured during antenatal clinic visits, the occurrence of HDP in Tanzanian population is rarely reported. Like with GDM, there was relatively high prevalence of HDP in the studied population. Overall prevalence was 7.7%, which was higher in the urban areas (8.9%) compared to the rural areas (5.3%). The observed risk factors for HDP in urban areas were advanced maternal age, increased MUAC and increased dietary diversity. HIV positive women were also at increased risk, with higher prevalence in the newly diagnosed compared to those already on anti-retroviral therapy. In the rural areas, the risk for HDP increased with age and gestational age.

Maternal risk factors for macrosomia and low birth weight were assessed in 466 women from Dar es Salaam who were followed-up for birth outcome by telephone (**Chapter 5**). Higher occurrence of macrosomia (5.9%) was observed compared to occurrence of low birth weight (3.6%) in women above 20 years. This shows existence of the double burden of malnutrition in the studied population even at the infancy stage. Women with GDM and those with a previous macrosomic child had increased risk for becoming a macrosomic infant, while those with HDP had an increased risk for stillbirths and low birth weight.

In **Chapter 6,** the opportunities and challenges for blood glucose screening in Tanzanian antenatal care were studied through a literature review and an urban health facility survey. The main challenge observed was the limited availability of both human and material resources. We found that diabetes screening during pregnancy is already in place using urine glucose testing, and it was regularly done in the urban setting. However, the sensitivity of an urinary glucose test in identifying women with GDM is low. The existing counselling and testing for HIV provides an opportunity to include blood glucose testing for GDM. However, the costs for GDM management are not known in Tanzania, so cost-benefit studies are needed before policies can be changed.

In **Chapter 7**, we summarised the main findings in this thesis and elaborated on the methodological considerations, public health importance and recommendations for

future research. The prevalence of GDM in Tanzania is higher than expected, specifically in the urban area, in this case Dar es Salaam. The main modifiable risk factor is overweight/obesity. Healthy lifestyle, including healthy diet and exercise, for prevention of overweight and obesity should be advocated specifically for women at reproductive age. Although there is still an ongoing debate worldwide on the usefulness of screening and on the diagnostic criteria for GDM, this should not be used as an excuse to postpone GDM testing in Tanzania, especially in urban women where type 2 diabetes, hypertension and overweight/obesity are recognized as highly prevalent disorders.

Samenvatting

De prevalentie van overgewicht/obesitas en type 2 diabetes neemt wereldwijd toe, ook in Afrika. Een veel genoemde verklaring voor deze waargenomen stijging is de verandering in leefstijl, zoals voeding en beweging, voornamelijk door verstedelijking. Zwangerschapsdiabetes is een risicofactor voor het optreden van type 2 diabetes op latere leeftijd, voor zowel moeder als kind. Vroegtijdige opsporing en behandeling verlaagt het risico op nadelige gevolgen van zwangerschapsdiabetes. Kennis over de omvang en de risicofactoren van zwangerschapsdiabetes zijn belangrijk om preventieve interventies beter te kunnen plannen, zodat de 'moeder-kind-cyclus' van type 2 diabetes doorbroken kan worden.

Het doel van dit proefschrift is om de prevalentie en de determinanten van zwangerschapsdiabetes in stedelijke en landelijke gebieden van Sub-Saharisch Afrika en specifiek voor Tanzania te bepalen.

Als eerste onderdeel van het project hebben we de prevalentie en risicofactoren van zwangerschapsdiabetes in Tanzania onderzocht, waarbij we stedelijke en landelijke gebieden met elkaar vergeleken (**Hoofdstuk 2**). Dit werd gedaan door middel van een dwarsdoorsnede onderzoek in verschillende geboorteklinieken waar vrouwen die de kliniek bezochten werden gevraagd om mee te doen. We zagen een hogere prevalentie van zwangerschapsdiabetes in stedelijke gebieden (8.4%) dan in landelijke gebieden (1.0%), waarbij de totale prevalentie (5.9%) veel hoger was vergeleken met gerapporteerde waardes in de jaren '90. De verschillen tussen landelijke en stedelijke gebieden kunnen onder andere het gevolg zijn van verschillen in lichamelijke beweging, aangezien de meeste vrouwen op het platteland betrokken zijn bij agrarisch werk, dat meer arbeidsintensief is. Een belaste familieanamnese voor type 2 diabetes, de aanwezigheid van overgewicht/obesitas gedefinieerd als bovenarmomtrek ≥ 28 cm en een doodgeboorte of miskraam in de voorgeschiedenis waren significant geassocieerd met aanwezigheid van zwangerschapsdiabetes. Ook werd bij vrouwen met bloedarmoede vaker zwangerschapsdiabetes gevonden dan bij vrouwen met normale haemoglobin concentraties. Belangrijk om op te merken is dat de prevalentie varieerde afhankelijk van de gebruikte diagnostische criteria. Wanneer de aanbevolen diagnostische criteria van de IADPSG werden gebruikt, met een lagere afkapwaarde voor nuchtere glucoseconcentratie, was de prevalentie van zwangerschapsdiabetes twee keer zo hoog (13.0%).

De prevalentie en gerapporteerde risicofactoren van zwangerschapsdiabetes in sub-Saharisch Afrika werden onderzocht aan de hand van een systematische review van de literatuur en een meta-regressie analyse van de resultaten (**Hoofdstuk 3**). Daarbij vonden we 22 studies, die waren uitgevoerd in slechts 6 van de 47 Afrikaanse landen beneden de Sahara, waarbij de meesten waren uitgevoerd in Nigeria. We vonden een hoge mate van heterogeniteit tussen de studies, die niet verklaard kon worden door de gebruikte variabelen in de meta-regressie analyse. De prevalentie was het hoogst bij vrouwen met een hoog risico, namelijk 14%. De risicofactoren die het meest frequent gerapporteerd werden waren: overgewicht en/of obesitas, een belaste familieanamnese voor type 2 diabetes, zwangerschapsdiabetes in een eerdere zwangerschap, een doodgeboorte in de voorgeschiedenis, een kind met hoog geboortegewicht (macrosomie) in een eerdere zwangerschap en een leeftijd boven de 30 jaar.

Een andere risicofactor voor complicaties tijdens of na de bevalling is het hebben van een hoge bloeddruk tijdens de zwangerschap. In **Hoofdstuk 4** hebben we de prevalentie van hoge bloeddruk tijdens de zwangerschap onderzocht. Tijdens de zwangerschap komen zwangerschapsdiabetes en hoge bloeddruk vaak tegelijk voor. Ondanks dat bloeddruk altijd wordt gemeten tijdens een bezoek aan een geboortekliniek, is er over het voorkomen van hoge bloeddruk in Tanzania weinig bekend. Net zoals voor zwangerschapsdiabetes kwam hoge bloeddruk relatief vaak voor in de bestudeerde onderzoekspopulatie. De prevalentie voor hoge bloeddruk was 7.7%, en was hoger in de stedelijke gebieden (8.9%) dan in de landelijke gebieden (5.3%). In stedelijke gebieden waren leeftijd van de moeder, een hogere bovenarmomtrek en een grotere variatie in voeding risicofactoren voor een hoge bloeddruk bij vrouwen. Ook hadden HIV-positieve vrouwen een hoger risico, waarbij in vrouwen die onlangs waren gediagnosticeerd vaker een hoge bloeddruk werd gemeten dan bij vrouwen die al antiretrovirale therapie kregen. In landelijke gebieden was het risico op hoge bloeddruk verhoogd met het toenemen van de leeftijd en de zwangerschapsduur.

Bij de deelnemende vrouwen uit Dar es Salaam (n=466) werd een follow-up onderzoek uitgevoerd naar geboorte-uitkomst, deels op basis van gegevens uit de kliniek, deels op basis van een telefonisch afgenomen vragenlijst. Met deze gegevens konden risicofactoren voor een r hoog of laag geboortegewicht bestudeerd worden (**Hoofdstuk 5**). Zowel een hoog (macrosomie) als een laag geboortegewicht kwamen voor bij vrouwen ouder dan 20 jaar; macrosomie kwam vaker voor (5.9%) dan een laag geboortegewicht (3.6%). Dit duidt erop dat de

zogenaamde 'dubbele belasting' van onder- en overvoeding ook terug te zien is in het stadium van de vroege kindertijd. Vrouwen met zwangerschapsdiabetes en vrouwen met een eerder zwaar kind hadden een verhoogd risico op het krijgen van een kind met hoog geboortegewicht, terwijl vrouwen met een hoge bloeddruk een verhoogd risico hadden op doodgeboorte of het krijgen van een kind met een laag geboortegewicht.

In **Hoofdstuk 6** hebben we de mogelijkheden en uitdagingen van diabetesscreening in Tanzaniaanse geboorteklinieken bestudeerd aan de hand van een literatuuroderzoek en een vragenlijstonderzoek bij gezondheidsinstellingen in Dar es Salaam. De voornaamste uitdaging voor screening bleek de beperkte beschikbaarheid van zowel menselijke als materiële middelen te zijn. Diabetesscreening wordt tijdens de zwangerschap voornamelijk gedaan door het testen van glucose in de urine; in de stedelijke gebieden gebeurde dit regelmatig. De gevoeligheid van de urine-glucose test is echter laag wanneer het gaat om het identificeren van vrouwen met zwangerschapsdiabetes. De bestaande begeleiding voor HIV en het testen daarvan biedt een mogelijkheid om het meten van bloedglucose eenvoudig mee te nemen. De kosten van het behandelen van zwangerschapsdiabetes in Tanzania zijn echter nog onbekend. Voordat het screeningsbeleid zou kunnen worden veranderd zijn er daarom eerst aanvullende economische evaluaties nodig.

In **Hoofdstuk 7** zijn de belangrijkste bevindingen van dit proefschrift samengevat en worden de methodologische beperkingen en de relevantie voor de volksgezondheid toegelicht. Ook worden er enkele aanbevelingen gegeven voor toekomstig onderzoek. De prevalentie van zwangerschapsdiabetes in Tanzania is hoger dan verwacht, met name in de stedelijke gebieden, in dit geval Dar es Salaam. De belangrijkste te beïnvloeden risicofactor is overgewicht/obesitas. Een gezonde leefstijl, waaronder gezonde voeding en voldoende beweging, en preventie van overgewicht en obesitas zou zeker bij vrouwen in de vruchtbare leeftijdsgroep moeten worden gestimuleerd. Ondanks dat er nog steeds een wereldwijd debat gaande is over de bruikbaarheid van screening en de diagnostische criteria van zwangerschapsdiabetes, zou dit geen excuus moeten zijn om het testen op diabetes tijdens de zwangerschap in Tanzania uit te stellen, zeker bij vrouwen in stedelijke gebieden waar type 2 diabetes, hoge bloeddruk en overgewicht/obesitas veel voorkomende aandoeningen zijn.

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AkwilinaWendelin-Mwanri

About the author

Biography

List of publications

Educational training

Biography

Akwilina Wendelin Mwanri was born on 2nd March 1969 in Kilimanjaro region, Tanzania. She completed advanced secondary education at Weruweru high school in 1990, majoring in Chemistry, Physics and Biology. In 1995, she graduated with a Bachelor degree in Food Science and Technology from Sokoine University of Agriculture. In 1996, she worked as a field research officer under Village Development Programme. From 1997 to 1999 she was employed by Tanga Education Society as a Secondary School Teacher teaching biology. In 2004, she completed her Masters of Science degree in Applied Human Nutrition from Nairobi University, Kenya which was sponsored by the German Academic Exchange Service (DAAD). From 2004 to 2006 Akwilina worked with the Ministry of Education – Tanzania as Education officer. From 2007 to date, she is working as a lecturer in the Department of Food Science and Technology at Sokoine University of Agriculture. In 2008, she did a Postgraduate Diploma in Food and Nutrition Security at Wageningen International, the Netherlands where she was awarded a postgraduate diploma certificate (with honours). It was during her postgraduate training when she developed interest in pursuing her PhD studies at Wageningen University. In 2010, she was competitively awarded a NUFFIC scholarship and started her sandwich PhD programme at Division of Human nutrition, Wageningen University which resulted in this PhD thesis entitled "Gestational diabetes mellitus in Tanzania – public health perspectives". During the course of this PhD study, she conducted a survey in selected urban and rural antenatal clinics where she did a glucose tolerance test in about 1000 pregnant women in Tanzania. She also attended several national and international courses and conferences in the field of human nutrition, diabetes and epidemiology within the education programme of the graduate school of VLAG. She is involved in several research activities including diabetes, infants and young child feeding practices and food and nutrition security. She also worked as a facilitator and co-facilitator in several sessions including Process for Promotion of Infants and Young child Feeding (ProPAN), nutrition in emergency, nutrition and economic development and nutrition and HIV/AIDS. Akwilina is married to Yosse Mwanri and she has one daughter and two sons.

List of publications and Abstracts presented in Conference

Publications

Mwanri AW, Kinabo JL, Ramaiya K, and Feskens EJM. Prevalence of gestational diabetes in Sub Saharan Africa: Systematic review and meta-regression analysis. *Tropical Medicine and International Health* (Submitted)

Mwanri AW, Kinabo JL, Ramaiya K, and Feskens EJM. High blood pressure and associated risk factors among women attending antenatal clinics in Tanzania. *Journal of hypertension* 2015 (accepted for publication)

Mwanri AW, Kinabo JL, Ramaiya K, and Feskens EJM. Prevalence of gestational diabetes in urban and rural Tanzania. *Diabetes research and clinical practice*, 2014; 103; 71-78

Mduma I, Msuya J, **Mwanri AW** and Yang RY. Carotenoids retention and *in vitro* iron bioavailability of traditional cowpea leaf dishes of rural Tanzania. *International Journal of food sciences and nutrition*. 2012; 63(3): 267–272

Mwanri AW, Kogi-Makau W and Laswai HS. Nutrients and anti-nutrients composition of raw, cooked and sundried sweet potato leaves. African Journal of Food, Agriculture, Nutrition and Development. 2011; 11(5): 5142-5156

Mamiro PS, Mbwaga AM, Mamiro DP, **Mwanri AW** and Kinabo JL. Nutritional quality and utilization of local and improved cowpea varieties in Iringa and Dodoma Regions, Tanzania.*African Journal of Food, Agriculture, Nutrition and Development*. 2011; 11(1): 4490-4506

Manuscripts under preparation

Mwanri AW, Kinabo JL, Ramaiya K, and Feskens EJM. Including blood glucose testing during antenatal clinic visits in Tanzania: Opportunities and challenges.

Mwanri AW, Epimack S, Kinabo JL, Ramaiya K, and Feskens EJM. Maternal risk factors for low birth weight and macrosomia in Tanzania.

Conference presentations

AW Mwanri, J. Kinabo, P. Mamiro, N. Bundala, J. Msuya, J. Ntwenya, K. Kulwa, A. Nombo, R. Mzimbiri, E. Macha, J. Picado, E. Chang. Improving Micronutrient Intake In Children: Results From Applying ProPAN In Zanzibar: oral presentation during Micronutrient Forum – Ethiopia. 2014.

Mwanri A, Feskens EJM, Kinabo JL, Ramaiya K. Is Dietary Diversity Score associated with blood glucose and hypertension among pregnant women in Tanzania? Abstract number P-1922, under Public Health Epidemiology, Poster presented during World Diabetes Congress: Melbourne, Australia. 2013.

Mwanri A, Feskens EJM, Kinabo JL, Ramaiya K. Blood glucose concentration and hypertension among pregnant women in Tanzania. Abstract number PD-1014, Under Diabetes in Special population, Poster Discussion Presented during world diabetes Congress Melbourne, Australia. 2013.

Mwanri AW, Feskens EJM, Kinabo JL, Ramaiya K. Risk factors for gestational diabetes mellitus in Morogoro urban, Tanzania. Abstract Number 1561, World Diabetes Congress, Dubai.2011.

Overview of completed training activities

Graduate School of VLAG

Discipline specific activities

Courses

- Advanced clinical course in management of diabetes, Stellenbosch , South Africa, 2012
- International course in evidence based nutrition, Antwerp, Belgium, 2013
- Public Health research in practice; how to evaluate interventions, VLAG, Wageningen, 2013

Meetings

- African Nutrition Epidemiology Conference, Nairobi, Kenya, 2010
- Nutrition Policy Mapping workshop, Dar es Salaam, Tanzania, 2012
- In-service nutrition training needs assessment workshop, Dar es Salaam, Tanzania, 2012
- In-Service nutrition training curriculum development, Dar es Salaam, Tanzania, 2012
- World Diabetes Congress, Melbourne, Australia, 2013
- Fibre in food and feed symposium, Wageningen University, 2013
- Micronutrient Forum conference, Addis Ababa, Ethiopia, 2014
- Gestational diabetes symposium, Dar es Salaam, Tanzania, 2015

General courses

- Information literacy including working with EndNote, Wageningen University Library, 2011
- Scientific publishing, Wageningen University, 2012
- Techniques for writing and presenting scientific paper, Wageningen University, 2012
- Assessments of infants and young child feeding using ProPAN tool, Tanzania, 2012
- African Nutrition Leadership Programme (ANLP), South Africa, 2013

Optional courses and activities

- Preparation PhD research proposal 2010/2011
- HNE course Epidemiology and Public Health, Wageningen, 2010
- HNE course Analytical Epidemiology, Wageningen, 2011
- PhD tour, Mexico and USA, School of VLAG, Wageningen University, 2011
- Staff seminar in Human Nutrition, Wageningen University, 2010/2013
- Staff/PhD seminar presentations, Sokoine University, 2013
- Paper clip discussions, Wageningen University, 2013/2014

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